UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450 Alexandria, Virginia 22313-1450 www.uspto.gov

## NOTICE OF ALLOWANCE AND FEE(S) DUE

26119

7590

08/24/2010

KLARQUIST SPARKMAN LLP 121 S.W. SALMON STREET SUITE 1600 PORTLAND, OR 97204

| EXAMINER          |              |  |  |  |
|-------------------|--------------|--|--|--|
| RIGGS II, LARRY D |              |  |  |  |
| ART UNIT          | PAPER NUMBER |  |  |  |

1631

DATE MAILED: 08/24/2010

|   | APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-----------------|-------------|----------------------|---------------------|------------------|
| Ī | 10/800.340      | 03/12/2004  | Lee Weng             | 3382-83763-01       | 9918             |

TITLE OF INVENTION: METHODS OF ANALYZING MULTI-CHANNEL PROFILES

| APPLN. TYPE    | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE   |
|----------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | NO           | \$1510        | \$300               | \$0                  | \$1810           | 11/24/2010 |

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

#### HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

#### PART B - FEE(S) TRANSMITTAL

## Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE

Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

or <u>Fax</u> (571)-273-2885

INSTRUCTIONS; This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where ap in m

| CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)  |   |  | Feet  | Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, mus have its own certificate of mailing or transmission. |                            |   |   |
|---|---|--|---|--|----------------------------|---|---|
| 26110   | 7500 0000   | /2010  | papa<br>have  | e its own certificate  | of mai                     | , such as an assignment<br>iling or transmission.   | it of formal drawing, must  |
| 121 S.W. SALM<br>SUITE 1600   | SPARKMAN LLI<br>ION STREET  | /2010<br>P   | I he<br>Stat<br>addi<br>tran  | reby certify that the  | is Fee(                    | e of Mailing or Transn<br>s) Transmittal is being<br>ficient postage for first<br>ISSUE FEE address<br>1) 273-2885, on the da | nission<br>deposited with the United<br>class mail in an envelope<br>above, or being facsimile<br>te indicated below. |
| PORTLAND, O   | OR 97204  |  |   |  |                            |   | (Depositor's name)  |
|   |   |  |   |  |                            |   | (Signature)   |
|   |   |  |   |  |                            |   | (Date)  |
| APPLICATION NO.   | FILING DATE   |  | FIRST NAMED INVENTOR  |  | ATTO                       | RNEY DOCKET NO.   | CONFIRMATION NO.  |
| 10/800,340  | 03/12/2004  |  | Lee Weng  |  | 3                          | 382-83763-01  | 9918  |
| TITLE OF INVENTION  | V: METHODS OF ANAL  | YZING MULTI-CHAN   | NEL PROFILES  |  |                            |   |   |
|   |   |  |   |  |                            |   |   |
| APPLN. TYPE   | SMALL ENTITY  | ISSUE FEE DUE  | PUBLICATION FEE DUE   | PREV. PAID ISSUI   | E FEE                      | TOTAL FEE(S) DUE  | DATE DUE  |
| nonprovisional  | NO  | \$1510   | \$300   | \$0  |                            | \$1810  | 11/24/2010  |
| EXAM  | MINER   | ART UNIT   | CLASS-SUBCLASS  |  |                            |   |   |
| RIGGS II,   | LARRY D   | 1631   | 702-019000  |  |                            |   |   |
| 1. Change of correspond   | ence address or indicatio   | n of "Fee Address" (37   | 2. For printing on the p  | atent front page, lis  | st                         |   |   |
| CFR 1.363).  ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.  ☐ "Fee Address" indication (or "Fee Address" Indication form |   |  | (1) the names of up to 3 registered patent attorneys or agents OR, alternatively,  (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to |  |                            |   |   |
|   | 02 or more recent) attach   |  | 2 registered patent atto<br>listed, no name will be   | rneys or agents. If :  | no nam                     | ie is 3   |   |
| 3. ASSIGNEE NAME A  | ND RESIDENCE DATA   | A TO BE PRINTED ON   | I<br>THE PATENT (print or typ   | ne)  |                            |   |   |
| PLEASE NOTE: Un   | less an assignee is ident   | ified below, no assignee   | data will appear on the p<br>T a substitute for filing an   | atent. If an assign  | ee is ic                   | lentified below, the do   | cument has been filed for   |
| (A) NAME OF ASSI  | •   |  | (B) RESIDENCE: (CITY  | · ·  | COUNT                      | RY)   |   |
|   |   |  |   |  |                            |   |   |
| Please check the appropri   | riate assignee category or  | categories (will not be pr   | rinted on the patent): $\Box$   | Individual 🖵 Co  | orporati                   | on or other private gro   | up entity 🚨 Government  |
|   |   |  | b. Payment of Fee(s): (Plea   |  |                            |   |   |
| 4a. The following fee(s)  Issue Fee   | are submitted:  | 41   | A check is enclosed.  | ise iirst reappiy ai   | iy prev                    | Tousty paid issue fee s   | поми авоче)   |
| ☐ Publication Fee (No small entity discount permitted)  |   |  | Payment by credit card. Form PTO-2038 is attached.  |  |                            |   |   |
| Advance Order -   | # of Copies   |  | The Director is hereby overpayment, to Depo   | authorized to char<br>sit Account Numbe  | ge the :<br>er             | required fee(s), any def<br>(enclose an   | iciency, or credit any extra copy of this form).  |
| 5. Change in Entity Sta   | *   |  | _   |  |                            |   |   |
| • •   | ns SMALL ENTITY state   |  | d from anyone other than t  |  |                            |   |   |
| interest as shown by the  | records of the United Sta   | tes Patent and Trademark   | COffice.  | ne applicant, a regi   | siereu .                   | attorney or agent, or the   | assignee of other party in  |
| Authorized Signature  |   |  |   | Date   |                            |   |   |
| Typed or printed nam  | ne  |  |   |  |                            |   |   |
| This collection of inform   | nation is required by 37 (  | FR 1 311. The information  | on is required to obtain or r   | etain a benefit by t   | he nub                     | lic which is to file (and   | by the USPTO to process)  |
| an application. Confiden<br>submitting the complete<br>this form and/or suggest   | tiality is governed by 35 d application form to the ions for reducing this bu.<br>Jirginia 22313-1450. DC | U.S.C. 122 and 37 CFR<br>USPTO. Time will vary<br>rden, should be sent to th | 1.14. This collection is esty depending upon the individual Chief Information Office COMPLETED FORMS TO   | imated to take 12 r<br>idual case. Any co<br>cr. U.S. Patent and   | minutes<br>mment<br>Traden | s to complete, including<br>s on the amount of tin<br>nark Office, U.S. Depa  | g gathering, preparing, and<br>ne you require to complete<br>rtment of Commerce, P.O.                                 |

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.



## United States Patent and Trademark Office

UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450

P.O. Box 1450 Alexandria, Virginia 22313-1450 www.uspto.gov

| APPLICATION NO.            | FILING DATE    | FIRST NAMED INVENTOR            | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|----------------------------|----------------|---------------------------------|---------------------|------------------|
| 10/800,340                 | 03/12/2004     | Lee Weng                        | 3382-83763-01       | 9918             |
| 26119 75                   | 590 08/24/2010 |                                 | EXAM                | INER             |
| KLARQUIST SE               | PARKMAN LLP    | RIGGS II,                       | LARRY D             |                  |
| 121 S.W. SALMO             | N STREET       |                                 | ART UNIT            | PAPER NUMBER     |
| SUITE 1600<br>PORTLAND, OR | 97204          | 1631<br>DATE MAILED: 08/24/2010 |                     |                  |

# Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 378 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 378 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

|  | Application No.   | Applicant(s)   |                  |
|--|---|--|------------------|
|  | 10/800,340  | WENG, LEE  |                  |
| Notice of Allowability   | Examiner  | Art Unit   |                  |
|  | LARRY D. RIGGS II   | 1631   |                  |
|  | LANNI D. NIGOS II   | 1031   |                  |
| The MAILING DATE of this communication appeal All claims being allowable, PROSECUTION ON THE MERITS IS herewith (or previously mailed), a Notice of Allowance (PTOL-85) NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIOF of the Office or upon petition by the applicant. See 37 CFR 1.313 | (OR REMAINS) CLOSED in or other appropriate communication is su | this application. If not included nication will be mailed in due cou | rse. <b>THIS</b> |
| 1. $\boxtimes$ This communication is responsive to <u>amendments and arg</u>   | uments discussed in the tele                                    | phonic interview 6/8/2010.   |                  |
| 2. X The allowed claim(s) is/are <u>1-18, 20-30, 32-36, 38-57, 66, </u>  | 67, 70-105, 107-164 and 166                                     | S-188 .  |                  |
| <ul> <li>3. ☐ Acknowledgment is made of a claim for foreign priority ur</li> <li>a) ☐ All b) ☐ Some* c) ☐ None of the:</li> <li>1. ☐ Certified copies of the priority documents have</li> </ul>  |   | r (f).   |                  |
| □ Certified copies of the priority documents have     □ Certified copies of the priority documents have  |   | n No   |                  |
| 3. ☐ Copies of the certified copies of the priority documents have   |   |  | from the         |
| International Bureau (PCT Rule 17.2(a)).   | cuments have been received                                      | in this hational stage application                                   | nom the          |
| * Certified copies not received:   |   |  |                  |
| Applicant has THREE MONTHS FROM THE "MAILING DATE" noted below. Failure to timely comply will result in ABANDONN THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.  |   | a reply complying with the require                                   | ements           |
| 4. A SUBSTITUTE OATH OR DECLARATION must be subm INFORMAL PATENT APPLICATION (PTO-152) which give  |   |  | CE OF            |
| 5. CORRECTED DRAWINGS ( as "replacement sheets") mus   | st be submitted.  |  |                  |
| (a) ☐ including changes required by the Notice of Draftspers   | on's Patent Drawing Review                                      | ( PTO-948) attached  |                  |
| 1) 🔲 hereto or 2) 🔲 to Paper No./Mail Date   |   |  |                  |
| (b) ☐ including changes required by the attached Examiner's<br>Paper No./Mail Date   | s Amendment / Comment or  | in the Office action of  |                  |
| Identifying indicia such as the application number (see 37 CFR 1 each sheet. Replacement sheet(s) should be labeled as such in t   |   |  | k) of            |
| 6. DEPOSIT OF and/or INFORMATION about the depo attached Examiner's comment regarding REQUIREMENT  |   |  | the              |
|  |   |  |                  |
| Attachment(s) 1. ☐ Notice of References Cited (PTO-892)  | 5. ☐ Notice of Info   | ormal Patent Application   |                  |
| 2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)   |   | mmary (PTO-413),   |                  |
| 3. Information Disclosure Statements (PTO/SB/08),  | Paper No./N   | Mail Date<br>Amendment/Comment                                       |                  |
| Paper No./Mail Date <u>3/19/2010</u> 4. ☐ Examiner's Comment Regarding Requirement for Deposit   | 8. <b>⊠</b> Examiner's S  | Statement of Reasons for Allowar                                     | nce              |
| of Biological Material   | 9. 🔲 Other  | ,  |                  |
|  |   |  |                  |

Art Unit: 1631

## **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with attorney Gregory Maurer on 8/10/2010.

The application has been amended as follows:

Art Unit: 1631

#### Listing of Claims

- 1. (Currently Amended) A method for generating at least one errorcorrected experiment profile of at least one experiment profile in a plurality of pairs of
  profiles {A<sub>m</sub>, C<sub>m</sub>}, where m = 1, 2, ..., M, and M is the number of the pairs of profiles;
  and wherein, for each m ∈ {1, 2, ..., M}, A<sub>m</sub> is an experiment profile, and C<sub>m</sub> is a
  reference profile; and wherein {A<sub>m</sub>} represents experiment profiles in said plurality of
  pairs of profiles {A<sub>m</sub>, C<sub>m</sub>} and {C<sub>m</sub>} represents reference profiles in said plurality of pairs
  of profiles {A<sub>m</sub>, C<sub>m</sub>}, said method comprising:
- (a) calculating, on a suitably programmed computer, an average reference profile  $\mathcal{E}$  of said plurality of reference profiles  $\{C_m\}$  where m=1,2,...,M;
- (b) determining, on a suitably programmed computer, for at least one profile pair  $\{A_m, C_m\}$  where  $m \in \{1, 2, ..., M\}$  of said plurality of pairs of profiles  $\{A_m, C_m\}$  a differential reference profile,  $C_{diff}(m,k)$ , computed between  $C_m$  and  $C_n$  wherein said average reference profile C comprises data set  $\{C(k)\}$ :
- (c) via said differential reference profile determined for said profile pair, removing, on a suitably programmed computer, systematic cross-experiment error from an experiment profile A<sub>m</sub> of said at least one profile pair (A<sub>m</sub>, C<sub>m</sub>) where m ∈ {1, 2, ..., M} to generate a first error-corrected experiment profile A'<sub>m</sub> for each m ∈ {1, 2, ..., M}, wherein said experiment profile A<sub>m</sub> comprises a first data set, {A<sub>m</sub>(k)}, said reference profile C<sub>m</sub> comprises a second data set, said average reference profile C comprises data set (E-(k)); and said first error-corrected experiment profile A'<sub>m</sub> comprises data set

Application/Control Number: 10/800,340

Art Unit: 1631

(A'<sub>m</sub> (k)); wherein said first data set comprises measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of a plurality of different cellular constituents measured in a sample having been subject to a first condition, said second data set comprises measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents measured in a sample having been subject to a second condition; and wherein k = 1, 2, ..., N; k is an index of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements, or logarithm-based transformed measurements, wherein generating respective A'<sub>m</sub>(k) of said first error-corrected experiment profile A'<sub>m</sub> comprises subtracting

- (d) obtaining a data-set  $\{A''_m(k)\}$ , wherein obtaining said data set  $\{A''_m(k)\}$  comprises combining said-first error-corrected experiment profile  $A'_m$  with said experiment profile  $A_m$  using a weighing factor  $\{w(k)\}$ ,  $k=-1,2,\ldots,N$ , wherein w(k) is a weighing factor for the kth measurement; and
- (e) (d) outputting to a user, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying: said first error-corrected experiment profile A'<sub>m</sub>[[,]] or said data set {A'<sub>m</sub>(k)}, ra-second-crror-corrected experiment profile A''<sub>m</sub>, or said data set {A''<sub>m</sub>(k)}, wherein-said second error-corrected experiment profile A''<sub>m</sub> comprises said data set {A''<sub>m</sub>(k)}.

- 2. (Previously Presented) The method of claim 1, wherein said steps (b) and (c) are performed for each profile pair  $\{A_m, C_m\}$  where  $m \in \{1, 2, ..., M\}$ .
- 3. (Currently Amended) The method of claim 2, wherein each of said experiment profile A<sub>m</sub> and said reference profile C<sub>m</sub> comprises measurements, error-model-based transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents from the same experimental reaction.
- 4. (Previously Presented) The method of claim 3, wherein said  $\mathcal{C}(k)$  is calculated according to the equation

$$\mathcal{E}(k) = \frac{1}{M} \sum_{m=1}^{M} C_m(k)$$

wherein said differential reference profile is determined according to the equation

$$C_{diff}(m,k) = C_m(k) - C(k)$$

and wherein said first error-corrected experiment profile  $A'_{\infty}$  is generated according to the equation

$$A'_{m}(k) \simeq A_{m}(k) - C_{diff}(m,k)$$

wherein  $\{A_m(k)\}$  is said first data set of experiment profile  $A_m$ .

Art Unit: 1631

5. (Currently Amended) The method of claim 4, further comprising:

- (4) (e) calculating, for one or more remaining profile pairs out of said profile pairs ( $\Lambda_m$ ,  $C_m$ ), a respective second error-corrected experiment profile  $A^*_m$ ; and
- (e) (1) outputting to, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying; said respective second error-corrected experiment profile A"m or said a data set {A"m (k)}.
- 6. (Previously Presented) The method of claim 5, wherein said second error-corrected experiment profile A"<sub>m</sub> is calculated according to the equation

$$A_{m}^{n}(k) = (1-w(k)) \cdot A_{m}(k) + w(k) \cdot A_{m}^{r}(k).$$

7. (Currently Amended) The method of claim 6, further comprising determining said a weighing factor w(k) according to the equation

$$w(k) = 1 - e^{-\alpha s \left[\frac{2}{2\sqrt{3}}\right]^2}$$

where avg\_bkgstd is an average background standard error.

8. (Previously Presented) The method of claim 7, further comprising determining said avg\_bkgstd according to the equation

$$avg\_bkgstd = \frac{1}{n}\sum_{k=1}^{N} \begin{bmatrix} \frac{1}{2} & M \\ \frac{1}{2} & \sum bkgstd(m,k) \end{bmatrix}$$

Art Unit: 1631

where bkgsnl(m, k) is background standard error of  $C_m(k)$ .

- 9. (Previously Presented) The method of claim 4, further comprising determining errors  $\{\sigma'_m(k)\}$  of said data set  $\{A'_m(k)\}$  in said first error-corrected experiment profile  $A'_m$ .
- 10. (Previously Presented) The method of claim 9, further comprising determining said errors  $\{\sigma'_{\infty}(k)\}$  according to the equation

$$\sigma'_{m}(k) = \sqrt{\sigma_{m}^{2}(k) + mixed_{\sigma_{m}^{2}(k)} - 2 \cdot Cor(k) \cdot \sigma_{m}(k) \cdot mixed_{\sigma_{m}^{2}(k)}}$$

where  $\sigma_m(k)$  is the standard error of  $A_m(k)$ , the method further comprising determining  $mixed \equiv \sigma_m(k)$  according to the equation

$$mixed\_\sigma_m(k) = \frac{\sigma_m(k) + (N-1)\sigma_{ref}(k)}{N}$$

where 
$$\sigma_{ref}(k) = \sqrt{\frac{\frac{1}{N-1}\sum\limits_{m}^{M}\left(C_{m}(k) - \tilde{C}(k)\right)^{2}}$$

and where Cor(k) is a correlation coefficient between said experiment profile  $A_m$  and said reference profile  $C_m$ .

11. (Previously Presented) The method of claim 10, further comprising determining said Cor(k) according to the equation

$$Cor(k) = CorMax \cdot \left[1 - e^{-0.5 \cdot \left[\frac{C(k)}{\text{long} \cdot 2 \cdot \text{gard}}\right]^2}\right]$$

where CorMax is a number between 0 and 1.

12. (Previously Presented) The method of claim 7, further comprising determining errors  $\{\sigma''_m(k)\}$  of said data set  $\{A''_m(k)\}$  in said second error-corrected experiment profile  $A''_m$ .

§3. (Previously Presented) The method of claim 12, wherein said errors  $\{\sigma''_m(k)\}$  are determined according to the equation

$$\sigma''_{m}(k) = \sqrt{[1 - w(k)] \cdot \sigma_{m}^{2}(k) + w(k)\sigma'_{m}^{2}(k)}$$

where  $\sigma_m(k)$  is the standard error of  $A_m(k)$ , the method further comprising (i) determining  $\sigma'_m(k)$  according to the equation

$$\sigma'_{m}(k) = \sqrt{\sigma_{m}^{2}(k) + mixed_{s}\sigma_{m}^{2}(k) - 2 \cdot Cor(k) \cdot \sigma_{m}(k) \cdot mixed_{s}\sigma_{m}(k)}, \text{ and}$$

(ii) determining  $mixed = \sigma_m(k)$  according to the equation

$$mixed\_\sigma_m(k) = \frac{\sigma_m(k) + (M-1) \cdot \sigma_{ref}(k)}{M}$$

where 
$$\sigma_{ref}(k) = \sqrt{\frac{1}{M-1}} \sum_{m}^{M} (\mathcal{E}_{m}(k) - C(k))^{2}$$

and where Cor(k) is a correlation coefficient between said experiment profile  $A_m$  and said reference profile  $C_m$ .

Art Unit: 1631

14. (Previously Presented) The method of claim 13, further comprising determining said Cor(k) according to the equation

$$Cor(k) = CorMax \cdot \left[1 - e^{-0.5 \left[\frac{\overline{C}(k)}{ang_{satgard}}\right]^{2}}\right]$$

where CorMax is a number between 0 and 1.

- 15. (Previously Presented) The method of claim 2, wherein said experiment profile  $A_m$  and said reference profile  $C_m$  of each said profile pair  $\{A_m, C_m\}$  are measured in a two-channel microarray experiment.
- 16. (Previously Presented) The method of claim 15, wherein said reference profiles  $\{C_m\}$ , where m=1,2,...,M, are measured with samples labeled with a same label.
- 17. (Previously Presented) The method of claim 2, wherein at least one of said plurality of pairs of profiles  $\{A_m, C_m\}$  is a virtual profile.
- 18. (Currently Amended) The method of claim 1, wherein said plurality of pairs of profiles  $\{A_m, C_m\}$  are transformed profiles each comprising orror model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in data set  $\{A_m(k)\}$  and data set  $\{C_m(k)\}$ , respectively; and wherein said data set  $\{A_m(k)\}$  is said first data set, and

Art Unit: 1631

said data set {Cm(k)} is said second data set.

19. (Can@led)

20. (Currently Amended) The method of claim 1, further comprising:

measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents to

(a0) removing nonlinearity, prior to said calculating step (a), from

generate said plurality of pairs of profiles (Am, Cm) comprising said experiment

profile Am and reference profile Cm.

21. (Currently Amended) The method of claim 20, wherein said removing step (a0) comprises:

(a0i) calculating an average profile of pre-experiment profiles  $(A \frac{pre}{m})$  and pre-reference profiles  $\{C \frac{pre}{m}\}$ ; wherein each of said pre-experiment profiles comprises measurements, error-model based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents measured in said sample having been subject to said first condition, which when nonlinearity is removed therefrom, produces each said experiment profile  $A_m$ ; and wherein each of said pre-reference profiles comprises measurements, error-model-based transformed measurements, or logarithm-based transformed measurements, or logarithm-based transformed measurements.

Art Unit: 1631

sample having been subject to said second condition, which when nonlinearity is removed therefrom, produces each said reference profile C<sub>m</sub>; and

(a0ii) calculating first differences between each of said pre-experiment profiles  $\{A_m^{pre}\}$  and said average profile; calculating second differences between each of said pre-reference profiles  $\{C_m^{pre}\}$  and said average profile; adjusting, wherein the adjusting comprises correcting nonlinearity, each of said pre-experiment profiles  $\{A_m^{pre}\}$  based on said first differences between each of said pre-experiment profiles  $\{A_m^{pre}\}$  and said average profile, thereby generating each said experiment profile  $\{A_m^{pre}\}$  and said average profile, thereby generating each said experiment profile  $\{A_m^{pre}\}$  and adjusting, wherein the adjusting comprises correcting nonlinearity, each of pre-reference profiles  $\{C_m^{pre}\}$  based on said second differences between each of said pre-reference profiles  $\{C_m^{pre}\}$  and said average profile, thereby generating each said reference profile  $\{C_m^{pre}\}$  and said average profile, thereby generating each said reference profile  $\{C_m^{pre}\}$ 

22. (Currently Amended) The method of claim 21, further comprising calculating said first differences based on a first subset of said measurements, error-model based transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents in said pre-experiment profiles (A \frac{pre}{m}) and said average profile; and calculating said second differences based on a second subset of said measurements, error-model based transformed measurements of said

Art Unit: 1631

plurality of different cellular constituents in said pre-reference profiles  $\{C_m^{pre}\}$  and said average profile.

- 23. (Currently Amended) The method of claim 22, wherein said first subset consists of measurements, error-model based transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents that are ranked similarly between each of said pre-experiment profiles  $\{A_{m}^{pru}\}$  and said average profile, and said second subset consists of measurements; error-model based transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents that are ranked similarly between each of said pre-reference profiles  $\{C_{m}^{pre}\}$  and said average profile.
- 24. (Currently Amended) The method of claim 23, wherein said adjusting step (a0ii) is carried out by a method comprising:
- (iii) binning said first subset into a first plurality of bins, wherein each of said first plurality of bins consists of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in one of said pre-experiment profiles  $\{A_{n_k}^{pre}\}$  and said average profile having a value in a given range; and binning said second subset into a second plurality of bins, wherein each of said second plurality of bins consists

Art Unit: 1631

of measurements, error-model based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in one of said pre-reference profiles  $\{C_{m}^{pre}\}$  and said average profile having a value in a given range;

- (ii2) calculating, in each bin of said first plurality of bins, a first mean difference between a feature value of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said one of said pre-experiment profiles  $\{A_{m}^{pre}\}$  and a feature value of said average profile, and calculating a second mean difference between a feature value of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said one of said pre-reference profiles  $\{C_{m}^{pre}\}$  and a feature value of said average profile;
- (ii3) determining a first curve of said first mean difference as a first function of values of measurements, error-model-based transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents for said one of said pre-experiment profiles  $\{A_{m}^{pre}\}$ , wherein said first function is represented by, nonlinear  $A_{m}^{pre}$ ; and determining a second curve of said second mean difference as a second function of values of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements for said one of said

Art Unit: 1631

pre-reference profiles  $\{C_m^{pre}\}$ , wherein said second function is represented by  $nonlinear \_C_m^{pre}$ ; and

(ii4) adjusting each of said pre-experiment profiles  $(A \frac{pre}{m})$  according to the equation:

$$A_m(k) = A \frac{pre}{m}(k) - nonlinear A \frac{pre}{m}(k)$$

and adjusting each of said pre-reference profiles  $\{C\frac{prg}{m}\}$  according to the equation:

$$C_m(k) = C \frac{pre}{m} (k) - nonlinear \_C \frac{pre}{m} (k),$$

where  $k=1,\ldots,N$ ; and where  $A\frac{pre}{m}(k)$  and  $C\frac{pre}{m}(k)$  are data sets of each of said pre-experiment profiles  $\{A^{pre}_{m}\}$  and each of said pre-reference profiles  $\{C^{pre}_{m}\}$ , respectively; and where  $A_{m}(k)$  and  $C_{m}(k)$  are said first data set and said second data set, respectively.

25. (Currently Amended) The method of claim 1, further comprising:

(a0) normalizing, prior to said calculating step (a), measurements, errormodel based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in a pre-experiment profile  $A_m^{pre}$  and a pre-reference profile  $C_m^{pre}$  to generate said experiment profile  $A_m$  and said reference profile  $C_m$ , respectively.

Application/Control Number: 10/800,340

Art Unit: 1631

26. (Currently Amended) The method of claim 25, wherein said  $\langle ^0 \rangle$  normalizing step (a0) comprises normalizing a data set  $A_{m}^{prs}(k)$  and a data set  $C_{m}^{prs}(k)$ , according to the equations:

Page 15

$$A_m(k) \equiv \frac{A_m^{pre}(k) \cdot A_m^{pre} c_m^{pre}}{A_m^{pre}}$$

and

$$C_{m}(k) = \frac{c_{m}^{pre}(k) \cdot A_{m}^{pre}c_{m}^{pre}}{c_{m}^{pre}},$$

wherein said data sets  $A_{m}^{pre}(k)$  and  $C_{m}^{pre}(k)$  each comprises measurements, errormodel-based transformed measurements, or logarithm-based transformed
measurements of said plurality of different cellular constituents, where  $A_{m}^{pre}$  is an
average of measurements, error-model-based transformed measurements, or
logarithm-based transformed measurements of said plurality of different cellular
constituents in said  $A_{m}^{pre}(k)$ , and  $C_{m}^{pre}$  is an average of measurements, error-modelbased transformed measurements, or logarithm-based transformed measurements
of said plurality of different cellular constituents in said  $C_{m}^{pre}(k)$ , wherein  $A_{m}(k)$  is
said first data set, wherein  $A_{m}(k)$  comprises normalized measurements or normalized
transformed measurements of said pre-experiment profile  $A_{m}^{pre}$ ; and  $C_{m}(k)$  is said
second data set wherein  $A_{m}(k)$  comprises normalized measurements or normalized
transformed measurements of said reference profile  $C_{m}^{pre}$ ; and wherein  $A_{m}^{pre}C_{m}^{pre}$ 

Art Unit: 1631

is an average calculated according to the equation

$$\overline{A_{m}^{pre}C_{m}^{pre}} = \frac{1}{2m} \sum_{m=1}^{M} \overline{A_{m}^{pre}} + \overline{C_{m}^{pre}}).$$

27. (Previously Presented) The method of claim 26, further comprising normalizing errors of said data sets  $\{A_{m}^{pre}(k)\}$  and  $\{C_{m}^{pre}(k)\}$ , respectively, according to the equations:

$$\sigma \stackrel{NA}{=} (k) = \frac{\sigma^{PRA}(k) \cdot \overline{A}^{PR} \sigma^{PR}}{\overline{A}^{PR}}$$

and

$$\sigma \frac{NC}{m}(k) = \frac{\sigma^{preC}(k) \cdot A^{pre}C^{pre}}{C^{pre}},$$

where  $\sigma \frac{preA}{m}(k)$  and  $\sigma \frac{preC}{m}(k)$  are the standard errors of  $A_{m}^{pre}(k)$  and  $C_{m}^{pre}(k)$ , respectively, and  $\sigma \frac{NA}{m}(k)$  and  $\sigma \frac{NC}{m}(k)$  are normalized standard errors of  $A_{m}(k)$  and  $C_{m}(k)$ , respectively.

28. (Previously Presented) The method of claim 27, further comprising normalizing background errors of said data sets  $\{A_{m}^{pre}(k)\}$  and  $\{C_{m}^{pre}(k)\}$ , respectively, according to the equations:

$$hkgstd {}^{NA}_{m}(k) = \frac{bkastd {}^{preA}(k) \cdot A {}^{pre} \cdot P^{pre}}{A {}^{pre}} {}^{m}_{m}$$

Art Unit: 1631

and

$$bkgstd \stackrel{NC}{=} (k) = \frac{bkasid^{preG}(k) A^{pre}C^{pre}}{C^{pre}}$$

where  $bkgstd \frac{preA}{m}(k)$  and  $bkgstd \frac{preC}{m}(k)$  are the standard background errors of  $A \frac{pre}{m}(k)$  and  $C \frac{pre}{m}(k)$ , respectively, and  $bkgstd \frac{NA}{m}(k)$  and  $bkgstd \frac{NC}{m}(k)$  are normalized standard background errors of  $A_m(k)$  and  $C_m(k)$ , respectively.

- (Currently Amended) The method of claim 28, further comprising calculating said averages  $\overline{A_m^{pre}}$  and  $\overline{C_m^{pre}}$  by excluding measurements, error-model-based transformed measurements of said plurality of different cellular constituents having a value among the highest 10% of said measurements, error-model-based transformed-measurements, or logarithm-based transformed-measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in said data sets  $\{A_m^{pre}(k)\}$  and  $\{C_m^{pre}(k)\}$ , respectively.
- 30. (Currently Amended) A method for generating at least one errorcorrected experiment profile of at least one experiment profile in a plurality of pairs
  of profiles {XA<sub>m</sub>, XC<sub>m</sub>}, XA<sub>m</sub> being an experiment profile, XC<sub>m</sub> being a reference
  profile, where m = 1, 2, ..., M, M is the number of pairs of profiles, said method
  comprising:
  - (a) processing, on a suitably programmed computer, said plurality of pairs of

Art Unit: 1631

profiles {XA<sub>m</sub>, XC<sub>m</sub>} to obtain a plurality of pairs of processed profiles {PA<sub>m</sub>, PC<sub>m</sub>}, PA<sub>m</sub> being a processed experiment profile, PC<sub>m</sub> being a processed reference profile, wherein said processing comprises normalizing at least one said experiment profile XA<sub>m</sub> and reference profile XC<sub>m</sub>;

- (b) calculating, on a suitably programmed computer, an average processed reference profile PC of processed reference profiles  $(PC_m)$ , where m = 1, 2, ..., M;
- (c) determining, on a suitably programmed computer, for at least one processed profile pair  $\{PA_m, PC_m\}$  where  $m \in \{1, 2, ..., M\}$  of said plurality of pairs of processed profiles  $\{PA_m, PC_m\}$ , where m = 1, 2, ..., M, a differential reference profile,  $\underline{PC_{diff}(m,k)}$ , computed between  $\underline{PC_m}$  and  $\underline{PC_m}$  wherein said average  $\underline{PC_{diff}(m,k)}$ , computed between  $\underline{PC_m}$  and  $\underline{PC_m}$  and  $\underline{PC_m}$  are  $\underline{PC_m}$  are  $\underline{PC_m}$ .
- (d) via said differential reference profile determined for said at least one processed profile pair, removing, on a suitably programmed computer, systematic cross-experiment error from a processed experiment profile  $PA_m$  of said at least one processed profile pair  $\{PA_m, PC_m\}$  where  $m \in \{1, 2, ..., M\}$  to generate a first error-corrected processed experiment profile  $PA_m$ ; wherein for each  $m \in \{1, 2, ..., M\}$ , said processed experiment profile  $PA_m$  comprises a first processed data set,  $\frac{\{PA_m(k)\}_k}{\{PA_m(k)\}_k}$  said processed reference profile  $PC_m$  comprises a second processed data set, said-average processed reference profile  $\frac{1}{4}$  comprises data set  $\frac{1}{4}$   $\frac{1}{$

Art Unit: 1631

 $XC_m$  comprises data set  $\{XC_m(k)\}$ , wherein said data set  $\{XA_m(k)\}$  comprises measurements of a plurality of different cellular constituents measured in a sample having been subject to a first condition, said data set  $\{XC_m(k)\}$  comprises measurements of said plurality of different cellular constituents measured in a sample having been subject to a second condition, and where k=1,2,...,N; k is an index of measurements of cellular constituents, N being the total number of measurements, wherein generating respective  $PA'_m$  (k) of said first error-corrected processed experiment profile  $PA'_m$  comprises subtracting  $PC_{diff}(m,k)$  from  $PA_m(k)$ ; and

(c) obtaining a data set  $(PA''_m(k))$ , wherein obtaining said data set  $(PA''_m(k))$  comprises combining said first error-corrected processed experiment profile  $PA'_m$  with said processed experiment profile  $PA_m$  using a weighing factor  $\{w(k)\}$ , k = 1, 2, ..., N, wherein w(k) is a weighing factor for the k'th measurement; and

(f) (e) outputting to a user, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying: said first error-corrected processed experiment profile PA'<sub>m</sub> [[.]] or said data set {PA'<sub>m</sub> (k)}, a second error-corrected processed experiment profile PA''<sub>m</sub> or said data set {PA''<sub>m</sub> (k)}, wherein said second error-corrected processed experiment profile PA''<sub>m</sub> comprises said data set {PA''<sub>m</sub> (k)}.

Art Unit: 1631

- 31. (Canceled)
- 32. (Currently Amended) The method of claim 30, wherein said normalizing is carried out according to the equations:

$$NA_{ss}(k) = \frac{XA_{ss}(k) \cdot \overline{XAZ}}{\overline{XA_{ss}}}$$

and

$$NC_{m}(k) \cong \frac{XC_{m}(k)TMC}{\overline{X}\overline{C_{m}}}$$

where  $\{NA_m(k)\}$  is said first data set of said processed experiment profile  $PA_m$ , and  $\{NC_m(k)\}$  is said second data set of said processed reference profile  $PC_m$ ; where  $\overline{XA_m}$  is an average of measurements, error-model based transformed measurements, er-logarithm-based transformed measurements of said plurality of different cellular constituents of said data set  $\{XA_m(k)\}$ , and  $\overline{XC_m}$  is an average of measurements, er-logarithm-based-transformed measurements, or logarithm-based-transformed measurements of said plurality of different cellular constituents of data set  $\{XC_m(k)\}$ ; and wherein  $\overline{XAC}$  is an average calculated according to the equation

$$\overline{XAC} = \frac{1}{2M} \sum_{m=1}^{M} (\overline{XA_{mi}} + \overline{XC_{mi}}).$$

33. (Previously Presented) The method of claim 32, further comprising normalizing errors of said experiment profile  $XA_m$  and reference profile  $XC_m$ 

Art Unit: 1631

according to the equations:

$$\sigma_{m}^{A}(k) = \frac{\sigma_{m}^{KA}(k) \overline{x_{ML}}}{\overline{x_{A_{m}}}}$$

and

$$\sigma_{m}^{C}(k) = \frac{\sigma_{NC}^{C}(k) \times k \times C}{N_{con}}$$

where  $\sigma_{m}^{XA}(k)$  and  $\sigma_{m}^{XC}(k)$  are the standard errors of  $XA_{m}(k)$  and  $XC_{m}(k)$ , respectively, and  $\sigma_{m}^{A}(k)$  and  $\sigma_{m}^{C}(k)$  are normalized standard errors of  $NA_{m}(k)$  and  $NC_{m}(k)$ , respectively.

34. (Previously Presented) The method of claim 33, further comprising normalizing background errors of said experiment profile XA<sub>m</sub> and reference profile XC<sub>m</sub> according to the equations:

$$bkgstd_m^A(k) = \frac{bkgstd_m^{XA}(k)\overline{XAC}}{X\overline{A_m}}$$

and

$$bkgstd_{m}^{C}(k) = \frac{mgstd_{m}^{RC}(k)^{TRC}}{RC_{m}}$$

where  $bkgstd\frac{XA}{m}$  (k) and  $bkgstd\frac{XC}{m}(k)$  are the standard background errors of  $XA_m(k)$  and  $XC_m(k)$ , respectively, and  $bkgstd\frac{A}{m}(k)$  and  $bkgstd\frac{C}{m}(k)$  are normalized standard

Art Unit: 1631

background errors of said  $NA_m(k)$  and said  $NC_m(k)$ , respectively.

- determining said averages  $\overline{XA_m}$  and  $\overline{XC_m}$  excluding measurements of said plurality of different cellular constituents having a value among the highest 10% of said measurements, error model based transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents in said data sets  $\{XA_m(k)\}$  and  $\{XC_m(k)\}$ , respectively.
- 36. (Previously Presented) The method of claim 30, wherein said processing step (a) comprises:

normalizing each said experiment profile  $XA_m$  and reference profile  $XC_m$  to generate normalized data set  $\{NA_m(k)\}$  and normalized data set  $\{NC_m(k)\}$ , respectively;

transforming said normalized data set  $\{NA_m(k)\}$  to obtain a transformed data set  $\{TA_m(k)\}$ , where said transformed data set  $\{TA_m(k)\}$  is said first data set of said processed experiment profile  $PA_m$ ; and

transforming said normalized data set  $\{NC_m(k)\}$  to obtain a transformed data set  $\{TC_m(k)\}$ , where said transformed data set  $\{TC_m(k)\}$  is said second data set of said processed reference profile  $PC_m$ ;

wherein said transforming is carried out for an experiment according to equations

$$TA_{m}(k) = f(x) = \frac{\ln \left[ \frac{5^{2} + 5 \cdot a^{2} \cdot 1/4 \cdot m(k)}{\pi} + 2 \cdot \sqrt{c^{2} + 5^{2} \cdot 1/4 \cdot m(k) + 2^{2} \cdot (1/4 \cdot m(k))^{2}} \right]}{\pi} + d,$$

Application/Control Number: 10/800,340

Art Unit: 1631

for 
$$NA_m(k)>0$$

and

$$TC_{m}(k) = f(x) = \frac{\ln\left[\frac{x^{2}+2x^{2}M^{2}(k)}{a} + \frac{x^{2}+b^{2}NC_{m}(k) + a^{2}NC_{m}(k)}{a}\right]}{a} + d,$$
 for  $NC_{m}(k) > 0$ 

where d is described by equation

$$d = \frac{-\ln\left[\frac{k^2}{4} + 2\pi\right]}{4}$$

and where a is the fractional error coefficient of said experiment, b is the Poisson error coefficient of said experiment, and c is the standard deviation of background noise of said experiment.

## 37. (Canceled)

38. (Previously Presented) The method of claim 30, wherein said processing step (a) comprises:

normalizing each said experiment profile  $XA_m$  and reference profile  $XC_m$  to generate normalized data set  $\{NA_m(k)\}$  and normalized data set  $\{NC_m(k)\}$ , respectively;

transforming said normalized data set  $\{NA_m(k)\}$  to a new domain in which variance becomes a constant to obtain a transformed data set  $\{TA_m(k)\}$ ;

transforming said normalized data set  $\{NC_m(k)\}$  to the new domain in which variance becomes a constant to obtain a transformed data set  $\{TC_m(k)\}$ ; and

Art Unit: 1631

removing nonlinearity from each said transformed data sets  $\{TA_m(k)\}$  and  $\{TC_m(k)\}$ , respectively.

- 39. (Previously Presented) The method of claim 38, wherein said removing nonlinearity is carried out by a method comprising
- (a1) calculating an average transformed profile of transformed experiment profiles and transformed reference profiles, wherein each of said transformed experiment profiles contains a corresponding transformed data set  $\{TA_m(k)\}$ , and each of said transformed reference profiles contains a corresponding transformed data set  $\{TC_m(k)\}$ ; and
- (a2) calculating first differences between each of said transformed experiment profiles and said average transformed profile; calculating second differences between each of said transformed reference profiles and said average transformed profile; adjusting, wherein the adjusting corrects nonlinearity, each of said transformed experiment profiles based on said first differences between each of said transformed experiment profiles and said average transformed profile, and adjusting, wherein the adjusting corrects nonlinearity, each of said transformed reference profiles based on said second differences between each of said transformed reference profiles and said average transformed profile.
- 40. (Currently Amended) The method of claim 39, further comprising calculating said first differences based on the differences in a first subset of error-

Art Unit: 1631

model-based-transformed-measurements or logarithm-based transformed measurements of said plurality of different cellular constituents between each of said transformed experiment profiles and said average transformed profile, and calculating said second differences based on the differences in a second subset of transformed measurements of said plurality of different cellular constituents between each of said transformed reference profiles and said average transformed profile.

- 41. (Currently Amended) The method of claim 40, wherein each said first subset consists of error model based transformed measurements or logarithm based transformed measurements that are ranked similarly between each of said transformed experiment profiles and said average transformed profile, and each said second subset consists of error-model based transformed measurements or logarithm based transformed measurements that are ranked similarly between each of said transformed reference profiles and said average transformed profile.
- 42. (Currently Amended) The method of claim 41, wherein said adjusting step (a2) is carried out by a method comprising:
- (a2i) blanking said first subset into a plurality of bins, each said bin consisting of crror-model-based-transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents in one of said transformed experiment profiles and said average transformed profile having a value in a given range; and binning said second subset into a plurality of bins, each said bin

Art Unit: 1631

consisting of error-model-based-transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents in one of said transformed reference profiles and said average transformed profile having a value in a given range;

between a feature value of error-model-based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents in said one of said transformed experiment profiles and a feature value of said average transformed profile, and calculating a second mean difference between a feature value of transformed measurements of said plurality of different cellular constituents in said one of said reference profiles and a feature value of the average profile;

(a2iii) determining a first curve of said first mean difference as a first function of values of error-model-based transformed measurements or logarithm based transformed measurements of said plurality of different cellular constituents for said one of said transformed experiment profiles, wherein said first function is represented by nonlinear\_TA<sub>m</sub>, and determining a second curve of said second mean difference as a second function of values of transformed measurements of said plurality of different cellular constituents for said one of said transformed reference profiles, wherein said second function is represented by nonlinear\_TC<sub>m</sub>; and

(a2iv) computing corrected transformed measurements of said plurality of different cellular constituents in each said transformed data set  $\{TA_m(k)\}$ , according to

Art Unit: 1631

the equation:

$$TA_{m}^{\text{COTT}}(k) = TA_{m}(k) - nonlinear\_TA_{m}(k),$$

and computing corrected transformed measurements of said plurality of different cellular constituents in each said transformed data set  $\{TC_m(k)\}$ , according to the equation:

$$TC_{m}^{corr}(k) = TC_{m}(k) - nonlinear \_TC_{m}(k),$$

where k=1,...,N; and where  $\{TA\frac{corr}{m}(k)\}$  is said first processed data set of said processed experiment profile  $PA_m$ , and  $\{TC\frac{corr}{m}(k)\}$  is said second processed data set of said processed reference profile  $PC_m$ .

- 43. (Currently Ameuded) The method of claim 42, wherein said processed experiment profile PA<sub>m</sub> and said processed reference profile PC<sub>m</sub> comprise error-model-based transformed measurements or logarithm based transformed measurements of said plurality of different cellular constituents from the same experimental reaction.
- 44. (Currently Amended) The method of claim 43, further comprising calculating  $P\overline{G}(k)$  according to the equation

$$\overline{PC}(k) = \frac{1}{\kappa} \sum_{m=1}^{M} PC_{m}(k),$$

wherein  $\{PC_m(k)\}$  comprises error-model-based-transformed-measurements-or logarithm-based transformed measurements from said second processed data

Art Unit: 1631

set  $\{TC\frac{corr}{m}(k)\}$  and calculating said differential reference profile according to the equation

$$PC_{diff}(m,k) = PC_{m}(k) - PC(k)$$

and wherein said first error-corrected profile is calculated according to the equation

$$PA'_{m}(k) = PA_{m}(k) - PC_{diff}(m, k),$$

wherein  $\{PA_m(k)\}$  comprises error-model-based-transformed-measurements or logarithm-based transformed measurements from said first data set  $\{TA_{nn}^{COTT}(k)\}$ .

- 45. (Previously Presented) The method of claim 44, further comprising
- (d) calculating for each processed profile pair  $\{PA_m, PC_m\}$ , where  $m \in \{1, 2, ..., M\}$ , a second error-corrected experiment profile  $PA''_m$  comprising data set  $\{PA''_m(k)\}$  by combining said first error-corrected experiment profile  $PA'_m$  with said processed experiment profile  $PA_m$  using a weighing factor  $\{w(k)\}$ , k = 1, 2, ..., N, wherein w(k) is a weighing factor for the Rth measurement.
- 46. (Previously Presented) The method of claim 45, wherein said second error-corrected experiment profile  $PA''_m$  is calculated according to the equation  $PA''_m(k) = (1-w(k)) \cdot PA_m(k) + w(k)PA'_m(k).$
- 47. (Previously Presented) The method of claim 46, further comprising determining said weighing factor according to the equation

Art Unit: 1631

$$w(k) = 1 - e^{-\alpha s \left[\frac{\sqrt{\kappa}(k)}{\log_2 \kappa \log_2 m}\right]^2}$$

where avg\_bkgstd is an average background standard error.

48. (Previously Presented) The method of claim 47, further comprising determining said avg\_bkgstd according to the equation

$$avg\_bkgsid = \frac{1}{N} \sum_{k=1}^{N} \left[ \frac{1}{N} \sum_{m=1}^{M} bkgstd(m,k) \right]$$

where bkgstd (m, k) is background standard error of  $PC_m$  (k).

- 49. (Previously Presented) The method of claim 44, further comprising determining errors  $\{P\sigma'_m\}$  of said first error-corrected experiment profile  $\{PA'_m\}$ , wherein said  $\{P\sigma'_m\}$  comprises error data set  $\{P\sigma'_m(k)\}$ .
- 50. (Previously Presented) The method of claim 49, further comprising determining said error data set  $\{P\sigma'_m(k)\}$  according to the equation

$$\sigma'_{m}(k) = \sqrt{P\sigma_{m}^{2}(k) = mixed_{p\sigma_{m}^{2}(k) - 2Cor(k) \cdot P\sigma_{m}(k) \cdot mixed_{p\sigma_{m}(k)}}$$

where  $P\sigma_m(k)$  is the standard error of  $\Lambda_m(k)$ , and determining  $mixed P\sigma_m(k)$  according to the equation

$$mixed_P\sigma_m(k) = \frac{P\sigma_m(k) + (N-1)P\sigma_{ref}(k)}{M}$$

where

Page 30

Application/Control Number: 10/800,340

Art Unit: 1631

$$P\sigma_{ref}(k) = \sqrt{\frac{1}{M-1}} \sum_{m}^{M} (PC_m(k) - \overline{PC}(k))^2$$

and where Cor(k) is a correlation coefficient between said processed experiment profile  $PA_m$  and said processed reference profile  $PC_m$ 

51. (Previously Presented) The method of claim 50, wherein said Cor(k) is determined according to the equation

$$Cor(k) = CorMax \cdot \left[1 - e^{-0.5 \left| \frac{K_{co}}{2 + a \cdot N_{cor}} \right|^{2}} \right]$$

where CorMax is a number between 0 and 1.

- 52. (Previously Presented) The method of claim 51, further comprising determining errors  $\{P\sigma^n_m\}$  of said second error-corrected experiment profile  $\{PA^n_m\}$  wherein said  $\{P\sigma^n_m\}$  comprises error data set  $\{P\sigma^n_m(k)\}$ .
- 53. (Previously Presented) The method of claim 52, further comprising determining said error data set  $\{P\sigma^*_{m}(k)\}$  according to the equation

$$P\sigma_{m}(k) = \sqrt{[1-w(k)] \cdot P\sigma_{m}^{2}(k) + w(k)P\sigma_{m}^{2}(k)}$$

where  $P\sigma_m(k)$  is the standard error of  $PA_m(k)$ , and further comprising determining  $P\sigma'_m(k)$  according to the equation

Application/Control Number: 10/800,340

Art Unit: 1631

$$P\sigma'_{m}(k) = \sqrt{P\sigma_{m}^{2}(k) + mixed_{po_{m}^{2}(k) - 2 \cdot Cer(k) \cdot P\sigma_{m}(k) \cdot mixed_{po_{m}(k)}},$$

Page 31

and

 $\langle m \rangle$ 

further comprising determining mixed  $P\sigma_m(k)$  according to the equation

$$mixed\_P\sigma_m(k) = \frac{P\sigma_m(k) + (N-1)P\sigma_{ref}(k)}{N}$$

where

$$P\sigma_{ref}(k) = \sqrt{\frac{1}{M-1} \sum_{m}^{M} (PC_{rm}(k) - P\overline{C}(k))^{2}}$$

and where Cor(k) is a correlation coefficient between said processed experiment profile  $PA_m$  and said processed reference profile  $PC_m$ .

54. (Previously Presented) The method of claim 53, further comprising determining said Cor(k) according to the equation

$$Cor(k) = CorMax \cdot \left[1 - s^{-0.9 \left[\frac{FC(k)}{crg_s Magned}\right]^2}\right]$$

where CorMax is a number between 0 and 1.

- 55. (Previously Presented) The method of claim 54, wherein each said pair of profiles XA<sub>m</sub> and XC<sub>m</sub> comprise measurements of said plurality of different cellular constituents from a two-channel microarray experiment.
  - 56. (Previously Presented) The method of claim 55, wherein said reference

Art Unit: 1631

profiles  $\{XC_m\}$ ,  $m=1,2,\ldots,M$ , are measured with samples labeled with a same label.

57. (Previously Presented) The method of claim 56, wherein at least one of said pairs of profiles  $\{XA_m, XC_m\}$  is a virtual profile.

- 58. (Canceled)
- 59. (Canceled)
- 60. (Canceled)
- 61. (Canceled)
- 62. (Canceled)
- 63. (Canceled)
- 64. (Canceled)
- 65. (Canceled)
- 66. (Currently Amended) A method for generating at least one error-corrected experiment profile of at least one experiment profile  $A_m$ , where  $m \in \{1, 2, ..., M\}$  in at least one of a plurality of pairs of profiles  $\{A_m, C_m\}$ ,  $A_m$  being an experiment profile,  $C_m$  being a reference profile, where m = 1, 2, ..., M, M is the number of pairs of profiles, said method comprising:

via a differential reference profile  $\underline{C_{dif}(m,k)}$  calculated between  $C_m$  and an average reference profile C, wherein said average reference profile  $\overline{C}$  comprises  $\underline{C(k)}$ . removing, on a suitably programmed computer, systematic cross-

Art Unit: 1631

experiment error from said experiment profile  $A_m$  for profile pair  $\{A_m, C_m\}$  where m€ {1, 2, ..., M} to generate a first error-corrected experiment profile A'm; wherein said average reference profile C is an average of reference profiles  $\{C_m\}$ , m = 1, 2. ..., M; wherein for each  $m \in \{1, 2, ..., M\}$ , said first error-corrected experiment profile  $A'_m$  comprises data set  $\{A'_m(k)\}$ , said experiment profile  $A_m$  comprises data set  $\{A_m(k)\}$ , and said reference profile  $C_m$  comprises data set  $\{C_m(k)\}$ , and said average reference profile & comprises data set (& (k)), wherein said data set {A<sub>m</sub>(k)} comprises measurements, error-model-based-transformed measurements, or logarithm-based transformed measurements of a plurality of different cellular constituents measured in a sample having been subject to a first condition, said thu set {C<sub>m</sub>(k)} comprises measurements, error-model-based transformed measurements, or logarithm-based transformed-measurements of said plurality of different cellular constituents measured in a sample having been subject to a second condition, wherein k = 1, 2, ..., N; k is an index of measurements, error-modelbased transformed-measurements, or logarithm-based transformed measurements of cellular constituents, N being the total number of measurements, wherein generating respective A' (k) of said first error-corrected experiment profile A' m comprises subtracting Case(m,k) from A. (k):

obtaining a data-set  $\{A''_m(k)\}_{\ell}$  wherein obtaining said data set  $\{A''_m(k)\}_{\ell}$  comprises combining said first error corrected experiment profile  $A'_m$  with said experiment profile  $A_m$  using a weighing factor  $\{w(k)\}_{\ell}$  k = 1, 2, ..., N, wherein w(k) is a weighing factor for the k'th measurement; and

Application/Control Number: 10/800,340

Art Unit: 1631

outputting to a user, a user interface device, a computer readable storage medium, or a local of remote computer system; or displaying: said first error-corrected experiment profile A'<sub>m</sub>[[,]] or said data set {A'<sub>m</sub>(k)}, a second error-corrected experiment profile A''<sub>m</sub> or said data set {A''<sub>m</sub>(k)}, wherein said second error-corrected experiment profile A''<sub>m</sub> comprises said data set {A''<sub>m</sub>(k)}.

Page 34

67. (Previously Presented) The method of claim 18, further comprising obtaining said transformed measurements of said data set  $\{C_m(k)\}$  for an experiment according to the equations:

$$A_m(k) = f(x) = \frac{in^{\left[\frac{b^2+2-a^2-3.5n_m(b)}{a}+2\sqrt{c^2+b^2-3.6n_m(b)}+a^2-[3.6n_m(b)]^2\right]}}{a} + d,$$
 for  $XA_m(k) > 0$ 

and

$$C_{m}(k) = f(x) = \frac{4\pi \left[\frac{8^{2}+x-x^{2}-XC_{01}(k)}{x}+2\sqrt{c^{2}+b^{2}-XC_{01}(k)+x^{2}-4XC_{m}(k))^{2}}\right]}{c} + d$$
for  $XC_{m}(k) > 0$ 

where  $\{XA_m(k)\}$  and  $\{XC_m(k)\}$  are data sets comprising measurements of said plurality of different cellular constituents that when transformed produce said transformed measurements of said plurality of different cellular constituents of said data set  $A_m(k)$  and said data set  $C_m(k)$ , respectively, where d is described by the equation:

Art Unit: 1631

and where a is the fractional error coefficient of said experiment, b is the Poisson error coefficient of said experiment, and c is the standard deviation of background noise of said experiment.

- 68. (Canceled)
- 69. (Canceled)
- 70. (Previously Presented) The method of claim 30, wherein said processing comprises:

normalizing, transforming, and/or removing nonlinearity from measurements of said plurality of cellular constituents of said data set  $\{XA_m(k)\}$  of said experiment profile  $XA_m$ , and from measurements of said plurality of cellular constituents of said data set  $\{XC_m(k)\}$  of said reference profile  $XC_m$ .

71. (Currently Amended) A computer program product for use in conjunction with a computer having a processor and a memory connected to the processor, said computer program product comprising a computer readable storage medium having a computer program mechanism encoded thereon, wherein said computer program mechanism may be loaded into the memory of said computer and

Art Unit: 1631

cause said computer to carry out a method for generating at least one error-corrected experiment profile of at least one experiment profile in a plurality of pairs of profiles  $\{A_m, C_m\}$ , where m = 1, 2, ..., M, and M is the number of the pairs of profiles; and wherein, for each  $m \in \{1, 2, ..., M\}$ ,  $A_m$  is an experiment profile, and  $C_m$  is a reference profile; and wherein  $\{A_m\}$  represents experiment profiles in said plurality of pairs of profiles  $\{A_m, C_m\}$  and  $\{C_m\}$  represents reference profiles in said plurality of pairs of profiles  $\{A_m, C_m\}$  said method comprising:

- (a) calculating, on a computer, an average reference profile  $\mathcal{L}$  of said plurality of reference profiles  $\{C_m\}$  where m=1,2,...,M;
- (b) determining, on a computer, for at least one profile pair  $\{A_m, C_m\}$  where  $m \in \{1, 2, ..., M\}$  of said plurality of pairs of profiles  $\{A_m, C_m\}$  a differential reference profile  $C_{diff}(m,k)$  computed between  $C_m$  and  $C_m$  wherein said average reference profile  $\overline{C}$  comprises data set  $\{\overline{C}(k)\}$ :
- (c) via said differential reference profile determined for said profile pair, removing, on a computer, systematic cross-experiment error from an experiment profile  $A_m$  of said at least one profile pair  $\{A_m, C_m\}$  where  $m \in \{1, 2, ..., M\}$  to generate a first error-corrected experiment profile  $A'_m$  for each  $m \in \{1, 2, ..., M\}$ , wherein said experiment profile  $A_m$  comprises a first data set  $\{A_m(k)\}_{k=1}^m$ , said reference profile  $C_m$  comprises a second data set, said average reference profile C comprises data set  $\{C'_m, C'_m\}_{k=1}^m$ , and said first error-corrected experiment profile  $A'_m$  comprises data set  $\{A'_m, C'_m\}_{k=1}^m$ , wherein said first data set comprises measurements; error-model based transformed

Application/Control Number: 10/800,340

Art Unit: 1631

measurements, or logarithm based transformed measurements of a phurality of different cellular constituents measured in a sample having been subject to a first condition, said second data set comprises measurements, error model-based transformed measurements, or logarithm based transformed measurements of said phurality of different cellular constituents measured in a sample having been subject to a second condition; and wherein k × 1, 2, ..., N; k is an index of measurements, error-model-based transformed measurements, or logarithm based transformed measurements of said phurality of different cellular constituents, N being the total number of measurements, error-model-based-transformed measurements, or logarithm-based transformed measurements, wherein generating respective  $A'_{m}(k)$  of said first error-corrected experiment profile  $A'_{m}$  comprises subtracting  $C_{Site}(m,k)$  from  $A_{m}(k)$ :

Page 37

(d) obtaining a data set  $\{\Lambda^{u}_{m}(k)\}$  by combining said first-error-corrected experiment profile  $\Lambda^{l}_{m}$  with said experiment profile  $\Lambda_{m}$  using a weighing factor  $\{w(k)\}, k=1,2,\ldots,N,$  wherein w(k) is a weighing-factor-for-the k-th measurement; and

(e) (d) outputting to a user, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying: said first error-corrected experiment profile A'<sub>m</sub>[[,]] or said data set {A'<sub>m</sub>(k)}, a second-error corrected experiment profile A''<sub>m</sub>, or said data set {A''<sub>m</sub>(k)}, wherein said second-error corrected experiment profile A''<sub>m</sub> comprises said data set {A''<sub>m</sub>(k)}.

- 72. (Previously Presented) The computer program product of claim 71, wherein said steps (b) and (c) are performed for each profile pair  $\{A_m, C_m\}$  where  $m \in \{1, 2, ..., M\}$ .
- 73. (Currently Amended) The computer program product of claim 72, wherein each of said experiment profile A<sub>m</sub> and said reference profile C<sub>m</sub> comprises measurements, error model-based-transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constiments from the same experimental reaction.
- 74. (Previously Presented) The computer program product of claim 73, wherein said C/k is calculated according to the equation

$$\mathcal{E}(k) = \frac{1}{M} \sum_{m=1}^{M} C_m(k)$$

wherein said differential reference profile is determined according to the equation

$$C_{aiff}(m,k) = C_m(k) - C(k)$$

and wherein said first error-corrected experiment profile A'm is generated according to the equation

$$A'_{m}(k) = A_{m}(k) - C_{diff}(m,k)$$

wherein  $\{A_m(k)\}$  is said first data set of experiment profile  $A_m$ .

Art Unit: 1631

75. (Currently Amended) The computer program product of claim 74, wherein the method further comprises:

- (d) (e) calculating, for one or more remaining profile pairs out of said profile pairs  $(\Lambda_m, C_m)$ , a respective second error-corrected experiment profile  $A''_m$ ; and
- (e) (f) outputting to, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying; said respective second error-corrected experiment profile A"<sub>m</sub> or said a data set {A"<sub>m</sub> (k)}.
- 76. (Previously Presented) The computer program product of claim 75, wherein said second error-corrected experiment profile  $\mathbf{A}''_{\mathbf{m}}$  is calculated according to the equation

$$A''_{m}(k) = \left(1 \cdot w(k)\right) \cdot A_{m}(k) + w(k) \cdot A'_{m}(k).$$

77. (Currently Amended) The computer program product of claim 76, wherein the method further comprises determining said a weighing factor w(k) according to the equation

$$w(k) = 1 - e^{-0.5 \left(\frac{2\pi q}{k_B}\right)^2}$$

where avg\_bkgstd is an average background standard error.

78. (Previously Presented) The computer program product of claim 77,

wherein the method further comprises determining said avg\_bkgstd according to the equation

$$avg\_bkgstd = \frac{1}{N} \sum_{k=1}^{N} \begin{bmatrix} \frac{1}{N} & M \\ \frac{1}{N} & \sum_{m=1}^{N} bkgstd(m,k) \end{bmatrix}$$

where bkgstd (m, k) is background standard error of  $C_m(k)$ .

- 79. (Previously Presented) The computer program product of claim 74, wherein the method further comprises determining errors  $\{\sigma'_{m}(k)\}$  of said data set  $\{A'_{m}(k)\}$  in said first error-corrected experiment profile  $A'_{m}$ .
- 80. (Previously Presented) The computer program product of claim 79, wherein the method further comprises determining said errors  $\{\sigma'_m(k)\}$  according to the equation

$$\sigma_{m}'(k) = \sqrt{\sigma_{m}^{2}(k) + mixed_{\sigma_{m}^{2}}(k) - 2 \cdot Cor(k) \cdot \sigma_{m}(k) \cdot mixed_{\sigma_{m}}(k)}$$

where  $\sigma_m$  (k) is the standard error of  $A_m(k)$ , the method further comprising determining  $mixed = \sigma_m$  (k) according to the equation

$$mixed_{\sigma_m}(k) = \frac{\sigma_m(k) + (M-1)\sigma_{r,sf}(k)}{N}$$

where 
$$\sigma_{ruj}(k) = \sqrt{\frac{1}{N-1}} \sum_{m}^{M} \left( \mathcal{C}_m(k) - \mathcal{C}(k) \right)^2$$

and where Cor(k) is a correlation coefficient between said experiment profile  $A_m$  and said reference profile  $C_m$ .

\$1. (Previously Presented) The computer program product of claim 80, wherein the method further comprises determining said Cor(k) according to the equation

$$Cor(k) = CorMax \cdot \left[1 - e^{-0.5 \cdot \left[\frac{\overline{L}(8)}{\text{Large Proved}}\right]^{2}}\right]$$

where CorMax is a number between 0 and 1.

- 82. (Previously Presented) The computer program product of claim 77. wherein the method further comprises determining errors  $\{\sigma^*_{m}(k)\}$  of said data set  $\{A^*_{m}(k)\}$  in said second error-corrected experiment profile  $A''_{m}$ .
- 83. (Previously Presented) The computer program product of claim 82, wherein said errors  $\{\sigma_m^*(k)\}$  are determined according to the equation

$$\sigma''_{m}(k) = \sqrt{[1 - w(k)] \cdot \sigma_{m}^{2}(k) + w(k)\sigma'_{m}^{2}(k)}$$

where  $\sigma_m(k)$  is the standard error of  $A_m(k)$ , the method further comprising (i) determining  $\sigma'_m(k)$  according to the equation

$$\sigma'_{m}(k) = \sqrt{\sigma_{m}^{2}(k) + mixed_{\sigma_{m}^{2}(k) - 2 \cdot Cor(k) \cdot \sigma_{m}(k) \cdot mixed_{\sigma_{m}}(k)}, \text{ and}}$$

(ii) determining  $mixed = \sigma_m(k)$  according to the equation

Application/Control Number: 10/800,340

Art Unit: 1631

$$mixed\_\sigma_m(k) = \frac{\sigma_m(k) + (M-1) \cdot \sigma_{ref}(k)}{M}$$

where 
$$\sigma_{rof}(k) = \sqrt{\frac{1}{N-1}} \sum_{m} (c_m(k) - \tilde{c}(k))^2$$

and where Cor(k) is a correlation coefficient between said experiment profile  $A_m$  and said reference profile  $C_m$ .

84. (Previously Presented) The computer program product of claim 83, wherein the method further comprises determining said Cor(k) according to the equation

where CorMax is a number between 0 and 1.

- 85. (Previously Presented) The computer program product of claim 72, wherein said experiment profile  $A_m$  and said reference profile  $C_m$  of each said profile pair  $\{A_m, C_m\}$  are measured in a two-channel microarray experiment.
- 86. (Previously Presented) The computer program product of claim 85, wherein said reference profiles  $\{C_m\}$ , where m = 1, 2, ..., M, are measured with samples labeled with a same label.

Art Unit: 1631

87. (Previously Presented) The computer program product of claim 72, wherein at least one of said plurality of pairs of profiles (Am, Cm) is a virtual profile.

- 88. (Currently Amended) The computer program product of claim 71, wherein said plurality of pairs of profiles  $\{A_m, C_m\}$  are transformed profiles each comprising error model-based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents in data set  $\{A_m(k)\}$  and data set  $\{C_m(k)\}$ , respectively; and wherein said data set  $\{A_m(k)\}$  is said first data set, and said data set  $\{C_m(k)\}$  is said second data set.
- 89. (Currently Amended) The computer program product of claim 71, wherein the method further comprises:
- (a0) removing nonlinearity, prior to said calculating step (a), from measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents to generate said plurality of pairs of profiles  $\{A_m, C_m\}$  comprising said experiment profile  $A_m$  and reference profile  $C_m$ .
- 90. (Correctly Amended) The computer program product of claim 89, wherein said removing step (a0) comprises:
- (a0i) calculating an average profile of pre-experiment profiles (A  $\frac{pre}{m}$ ) and pre-reference profiles (C  $\frac{pre}{m}$ ); wherein each of said pre-experiment profiles

Art Unit: 1631

logarithm based transformed measurements of said plurality of different cellular constituents measured in said sample having been subject to said first condition, which when nonlinearity is removed therefrom, produces each said experiment profile A<sub>m</sub>; and wherein each of said pre-reference profiles comprises measurements, error-model-based-transformed-measurements, or logarithm-based-transformed measurements of said plurality of different cellular constituents measured in said sample having been subject to said second condition, which when nonlinearity is removed therefrom, produces each said reference profile C<sub>m</sub>; and

(a0ii) calculating first differences between cach of said pre-experiment profiles  $\{A_m^{pre}\}$  and said average profile; calculating second differences between each of said pre-reference profiles  $\{C_m^{pre}\}$  and said average profile; adjusting, wherein the adjusting comprises correcting nonlinearity, each of said pre-experiment profiles  $\{A_m^{pre}\}$  based on said first differences between each of said pre-experiment profiles  $\{A_m^{pre}\}$  and said average profile, thereby generating each said experiment profile  $A_m$ ; and adjusting, wherein the adjusting comprises correcting nonlinearity, each of pre-reference profiles  $\{C_m^{pre}\}$  based on said second differences between each of said pre-reference profiles  $\{C_m^{pre}\}$  and said average profile, thereby generating each said reference profiles  $\{C_m^{pre}\}$  and said average

Art Unit: 1631

- 91. (Currently Amended) The computer program product of claim 90, wherein the method further comprises calculating said first differences based on a first subset of said measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in said pre-experiment profiles  $\{A_{m}^{pre}\}$  and said average profile; and calculating said second differences based on a second subset of said measurements; error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in said pre-reference profiles  $\{C_{m}^{pre}\}$  and said average profile.
- wherein said first subset consists of measurements, error-model-based-transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents that are ranked similarly between each of said pre-experiment profiles ( $A_{70}^{pre}$ ) and said average profile, and said second subset consists of measurements, error model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents that are ranked similarly between each of said pre-reference profiles ( $C_{70}^{pre}$ ) and said average profile.
  - 93. (Currently Amended) The computer program product of claim 92,

Art Unit: 1631

wherein said adjusting step (a0ii) is carried out by a method comprising:

(iii) binning said first subset into a first plurality of bins, wherein each of said first plurality of bins consists of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in one of said pre-experiment profiles  $\{A_{m}^{pre}\}$  and said average profile having a value in a given range; and binning said second subset into a second plurality of bins, wherein each of said second plurality of bins consists of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements, or logarithm-based transformed measurements constituents in one of said pre-reference profiles  $\{C_{m}^{pre}\}$  and said average profile having a value in a given range;

- (ii2) calculating, in each bin of said first plurality of bins, a first mean difference between a feature value of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said one of said pre-experiment profiles  $\{A_{m}^{pre}\}$  and a feature value of said average profile, and calculating a second mean difference between a feature value of measurements, error-model based transformed measurements, or logarithm-based transformed-measurements of said one of said pre-reference profiles  $\{C_{m}^{pre}\}$  and a feature value of said average profile:
- (ii3) determining a first curve of said first mean difference as a first function of values of measurements, error-model-based transformed measurements, or

Art Unit: 1631

logarithm-based-transformed-measurements of said plurality of different cellular constituents for said one of said pre-experiment profiles  $(A \frac{pre}{m})$ , wherein said first function is represented by,  $nonlinear A \frac{pre}{m}$ ; and determining a second curve of said second mean difference as a second function of values of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents for said one of said pre-reference profiles  $(C \frac{pre}{m})$ , wherein said second function is represented by  $nonlinear = C \frac{pre}{m}$ ; and

(ii4) adjusting each of said pre-experiment profiles  $\{A^{pre}_{m}\}$  according to the equation:

$$A_m(k) = A \frac{pre}{m}(k) - nonlinear A \frac{pre}{m}(k),$$

and adjusting each of said pre-reference profiles  $\{Crac{pre}{m}\}$  according to the equation:

$$C_m(k) = C \frac{pre}{m}(k) - nonlinear _C \frac{pre}{m}(k),$$

where  $k=1,\ldots,N$ ; and where  $A\frac{pre}{m}(k)$  and  $C\frac{pre}{m}(k)$  are data sets of each of said pre-experiment profiles  $\{A\frac{pre}{m}\}$  and each of said pre-reference profiles  $\{C\frac{pre}{m}\}$ , respectively; and where  $A_m(k)$  and  $C_m(k)$  are said first data set and said second data set, respectively.

94. (Currently Amended) The computer program product of claim 71,

Art Unit: 1631

wherein the method further comprises:

(a0) normalizing, prior to said calculating step (a), measurements, errormodel based transformed measurements, or logarithm-based transformed measurements of said plurately of different cellular constituents in a pre-experiment profile  $A_m^{pre}$  and a pre-reference profile  $C_m^{pre}$  to generate said experiment profile  $A_m$  and said reference profile  $C_m$ , respectively.

95. (Currently Amended) The computer program product of claim 94, wherein said normalizing step (a0) comprises normalizing a data set  $A_{m}^{pre}(k)$  and a data set  $C_{m}^{pre}(k)$ , according to the equations:

$$A_m(k) = \frac{4^{pre}(k) \cdot 4^{pre}c^{pre}}{4^{pre}} \stackrel{n}{=}$$

and

$$C_{m}(k) = \frac{c^{pre}(n) \sqrt{pre}/pre}{c^{\frac{m}{2}}},$$

wherein said data sets  $A_{m}^{pre}(k)$  and  $C_{m}^{pre}(k)$  each comprises measurements, errormodel-based transformed measurements, or logarithm-based transformed
measurements of said physicity of different cellular constituents, where  $A_{m}^{pre}$  is an average of measurements, error-model-based transformed measurements, er
logarithm-based-transformed measurements of said plurality of different cellular constituents in said  $A_{m}^{pre}(k)$ , and  $C_{m}^{pre}$  is an average of measurements, error-model-

based-transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in said  $C_m^{pre}(k)$ , wherein  $A_m(k)$  is said first data set, wherein  $A_m(k)$  comprises normalized measurements or normalized transformed measurements of said pre-experiment profile  $A_m^{pre}$ ; and  $C_m(k)$  is said second data set wherein  $A_m(k)$  comprises normalized measurements or normalized transformed measurements of said reference profile  $C_m^{pre}$ ; and wherein  $\overline{A_m^{pre}C_m^{pre}}$  is an average calculated according to the equation

$$\overline{A_{m}^{pre}C_{m}^{pre}} = \frac{1}{2N} \sum_{m=1}^{M} \overline{(A_{m}^{pre} + \overline{C_{m}^{pre}})}.$$

96. (Previously Presented) The computer program product of claim 95, wherein the method further comprises normalizing errors of said data sets  $\{A_{m}^{pre}(k)\}$  and  $\{C_{m}^{pre}(k)\}$ , respectively, according to the equations:

$$\sigma^{NA}_{m}(k) = \frac{\sigma^{mA_{(k)} \overline{A^{pm}} \sigma^{pm}}}{\overline{A^{pm}}}$$

and

$$\sigma \stackrel{NC}{m}(k) = \frac{\sigma^{proC(k)} A^{proCpro}}{\mathbb{Z}^{pro}},$$

where  $\sigma \frac{meA}{m}(k)$  and  $\sigma \frac{preC}{m}(k)$  are the standard errors of  $A_m^{pre}(k)$  and  $C_{mi}^{pre}(k)$ , respectively, and  $\sigma \frac{NA}{m}(k)$  and  $\sigma \frac{NC}{m}(k)$  are normalized standard errors of  $A_m(k)$  and

Art Unit: 1631

 $C_m(k)$ , respectively.

97. (Previously Presented) The computer program product of claim 96, wherein the method further comprises normalizing background errors of said data sets  $\{A_{m}^{pre}(k)\}$  and  $\{C_{m}^{pre}(k)\}$ , respectively, according to the equations:

$$bkgstd \frac{NA}{m}(k) = \frac{bkgssst}{4} \frac{pres}{m} \frac{pres}{m} \frac{e^{pre}}{m}$$

and

$$bkgstd \stackrel{NC}{m}(k) = \frac{\frac{bkgsvd^{preC}(k)}{m} \frac{pre_{c}pre}{m}}{c^{pre}}$$

where  $bkgsid \frac{pred}{m}(k)$  and  $bkgsid \frac{pred}{m}(k)$  are the standard background errors of  $A_m^{pre}(k)$  and  $C_m^{pre}(k)$ , respectively, and  $bkgsid \frac{NA}{m}(k)$  and  $bkgsid \frac{NC}{m}(k)$  are normalized standard background errors of  $A_m(k)$  and  $C_m(k)$ , respectively.

wherein the method further comprises calculating said averages  $A^{\frac{prg}{m}}$  and  $C^{\frac{prg}{m}}$  by excluding measurements, error model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents having a value among the highest 10% of said measurements, error model-based transformed measurements, or logarithm-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in said data sets

Art Unit: 1631

$$\{A_{m}^{pre}(k)\}$$
 and  $\{C_{m}^{pre}(k)\}$ , respectively.

- 69. (Currently Amended) A computer program product for use in conjunction with a computer having a processor and a memory connected to the processor, said computer program product comprising a computer readable storage medium having a computer program mechanism encoded thereon, wherein said computer program mechanism may be loaded into the memory of said computer and cause said computer to carry out a method for generating at least one error-corrected experiment profile of at least one experiment profile in a plurality of pairs of profiles  $\{XA_m, XC_m\}$ ,  $XA_m$  being an experiment profile,  $XC_m$  being a reference profile, where m = 1, 2, ..., M, M is the number of pairs of profiles, said method comprising:
- (a) processing, on a computer, said plurality of pairs of profiles  $\{XA_m, XC_m\}$  to obtain a plurality of pairs of processed profiles  $\{PA_m, PC_m\}$ ,  $PA_m$  being a processed experiment profile,  $PC_m$  being a processed reference profile, wherein said processing comprises normalizing at least one said experiment profile  $XA_m$  and reference profile  $XC_m$ ;
- (b) calculating, on a computer, an average processed reference profile FC of processed reference profiles  $\{PC_m\}$ , where m=1,2,...,M;
- (c) determining, on a computer, for at least one processed profile pair  $\{PA_m, PC_m\}$  where  $m \notin \{1, 2, ..., M\}$  of said plurality of pairs of processed profiles  $\{PA_m, PC_m\}$

Art Unit: 1631

 $PC_m$ }, where m = 1, 2, ..., M, a differential reference profile  $\underline{PC_{diff}(m,k)}$  computed between  $PC_m$  and  $\underline{PC_{wherein said average processed reference profile <math>\underline{PC_{comprises data set}(PC_{comprises data set$ 

(d) via said differential reference profile determined for said at least one processed profile pair, removing, on a computer, systematic cross-experiment error from a processed experiment profile  $PA_m$  of said at least one processed profile pair  $\{PA_m,$  $PC_m$  where  $m \in \{1, 2, ..., M\}$  to generate a first error-corrected processed experiment profile  $PA'_m$ ; wherein for each  $m \in \{1, 2, ..., M\}$ , said processed experiment profile  $PA_m$  comprises a first processed data set  $\{PA_m(K)\}$ , said processed reference profile PC<sub>m</sub> comprises a second processed data set, said average processed reference profile PC comprises data set (PC(k)), said first error-corrected processed experiment profile  $PA'_{m}$  comprises dataset  $\langle PA'_{m}(k) \rangle$ , said experiment profile XAm comprises data set {XAm(k)}, said reference profile XCm comprises data set {XCm(k)}, wherein said data set {XAm(k)} comprises measurements of a plurality of different cellular constituents measured in a sample having been subject to a first condition, said data set {XCm(k)} comprises measurements of said plurality of different cellular constituents measured in a sample having been subject to a second condition, and where k == 1, 2, ..., N; k is an index of measurements of cellular constituents. N being the total number of measurements, wherein generating respective PA', (k) of said first errorcorrected processed experiment profile PA'm comprises subtracting PCdiff(m,k)

Art Unit: 1631

## from PAn(k): and;

(v) obtaining data set  $\{PA''_m(k)\}$ , wherein obtaining said data set  $\{PA''_m(k)\}$  comprises combining said first error  $\{PA'_m\text{ velocity processed experiment profile }PA'_m$  with said processed-experiment profile  $PA_m$  using a weighing factor  $\{m(k)\}$ , k = 1, 2, ..., N, wherein m(k) is a weighing factor for a k-th measurement; and

- (f) (e) outputting to a user, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying: said first error-corrected processed experiment profile PA'<sub>m</sub> [[.]] or said data set {PA'<sub>m</sub> (k)}, a second error corrected processed experiment profile PA''<sub>m</sub> or said data set {PA'<sub>m</sub> (k)}, wherein said second error corrected processed experiment profile PA''<sub>m</sub> comprises said data set {PA''<sub>m</sub> (k)}.
- 100. (Previously Presented) The computer program product of claim 99, wherein said processing step (a) comprises normalizing each said experiment profile  $XA_m$  and reference profile  $XC_m$ .
- 101. (Currently Amended) The computer program product of claim 100, wherein said normalizing is carried out according to the equations:

$$NA_m(k) = \frac{RA_m(k)}{RA_m}$$

and

where  $\{NA_m(k)\}$  is said first data set of said processed experiment profile  $PA_m$ , and  $\{NC_m(k)\}$  is said second data set of said processed reference profile  $PC_m$ ; where  $\overline{XA_m}$  is an average of measurements, error model based transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents of said data set  $\{XA_m(k)\}$ , and  $\overline{XC_m}$  is an average of measurements; error model based transformed measurements; or logarithm based transformed measurements of said plurality of different cellular constituents of data set  $\{XC_m(k)\}$ ; and wherein  $\overline{XAC}$  is an average calculated according to the equation

$$\overline{XAC} = \frac{1}{2M} \sum_{m=1}^{M} (\overline{XA_m} + \overline{XC_m}).$$

102. (Previously Presented) The computer program product of claim 101, wherein the method further comprises normalizing errors of said experiment profile  $XA_m$  and reference profile  $XC_m$  according to the equations:

$$\sigma_{m}^{A}\left(k\right)=\frac{e^{\frac{\pi A}{m}\left(k\right)\cdot\widetilde{k}\widetilde{k}\widetilde{k}}}{\widetilde{\kappa}\widetilde{k}\widetilde{m}}$$

and

$$\sigma_m^C(k) = \frac{e^{XC}(k)}{m}$$

where  $\sigma_{m}^{XA}(k)$  and  $\sigma_{m}^{XC}(k)$  are the standard errors of  $XA_{m}(k)$  and  $XC_{m}(k)$ ,

respectively, and  $\sigma_m^A(k)$  and  $\sigma_m^C(k)$  are normalized standard errors of NA<sub>m</sub>(k) and NC<sub>m</sub>(k), respectively.

103. (Previously Presented) The computer program product of claim 102, wherein the method further comprises normalizing background errors of said experiment profile XA<sub>m</sub> and reference profile XC<sub>m</sub> according to the equations:

$$bkgstd\frac{A}{m}(k) = \frac{mgmi^{Xh}(n)XX}{x_m}$$

and

$$bkgstd_{m}^{G}(k) = \frac{bkgstd_{M}^{MG}(k)}{MG}$$

where  $bkgstd\frac{XA}{m}$  (ic) and  $bkgstd\frac{XC}{m}(k)$  are the standard background errors of  $XA_m(k)$  and  $XC_m(k)$ , respectively, and  $bkgstd\frac{A}{m}(k)$  and  $bkgstd\frac{C}{m}(k)$  are normalized standard background errors of said  $NA_m(k)$  and said  $NC_m(k)$ , respectively.

104. (Currently Amended) The computer program product of claim 102, wherein the method further comprises determining said averages  $\overline{XA_m}$  and  $\overline{XC_m}$  excluding measurements of said plurality of different cellular constituents having a value among the highest 10% of said measurements, error-model based transformed measurements of said plurality of

different cellular constituents in said data sets  $\{XA_m(k)\}$  and  $\{XC_m(k)\}$ , respectively.

105. (Previously Presented) The computer program product of claim 99, wherein said processing step (a) comprises:

normalizing each said experiment profile  $XA_m$  and reference profile  $XC_m$  to generate normalized data set  $\{NA_m(k)\}$  and normalized data set  $\{NC_m(k)\}$ , respectively;

transforming said normalized data set  $\{NA_m(k)\}$  to obtain a transformed data set  $\{TA_m(k)\}$ , where said transformed data set  $\{TA_m(k)\}$  is said first data set of said processed experiment profile  $PA_m$ ; and

transforming said normalized data set  $\{NC_m(k)\}$  to obtain a transformed data set  $\{TC_m(k)\}$ , where said transformed data set  $\{TC_m(k)\}$  is said second data set of said processed reference profile  $PC_m$ ;

wherein said transforming is carried out for an experiment according to equations

$$TA_{m}(k) = f(x) = \frac{\ln\left[\frac{b^{2} + s + a^{2} \cos (m(k))}{a} + 2 \cdot \int e^{2} + b^{2} \cdot NA_{m}(k) + a^{2} \cdot (NA_{m}(k))^{2}\right]}{a} + d,$$
 for  $NA_{m}(k) \ge 0$ 

and

$$\begin{split} TC_m\left(k\right) = f(x) = \frac{\ln\left[\frac{k^2 + 2 \cdot k^2 \cdot NC_m(k)}{2} + 2 \sqrt{k^2 + k^2 \cdot NC_m(k)} + \alpha^2 \cdot \left[k^2 \cdot C_m(k)\right]^2\right]}{n} + d, \\ \text{for } NC_m(k) > 0 \end{split}$$

where d is described by equation

$$d = \frac{\ln \left[\frac{5^2}{6^2} \cdot 12^2 c\right]}{a}$$

Art Unit: 1631

and where a is the fractional error coefficient of said experiment, b is the Poisson error coefficient of said experiment, and c is the standard deviation of background noise of said experiment.

106. (Canceled)

107. (Previously Presented) The computer program product of claim 99, wherein said processing step (a) comprises:

normalizing each said experiment profile  $XA_m$  and reference profile  $XC_m$  to generate normalized data set  $\{NA_m(k)\}$  and normalized data set  $\{NC_m(k)\}$ , respectively;

transforming said normalized data set  $\{NA_m(k)\}$  to a new domain in which variance becomes a constant to obtain a transformed data set  $\{TA_m(k)\}$ ;

transforming said normalized data set  $\{NC_m(k)\}$  to a new domain in which variance becomes a constant to obtain a transformed data set  $\{TC_m(k)\}$ ; and removing nonlinearity from each said transformed data sets  $\{TA_m(k)\}$  and  $\{TC_m(k)\}$ , respectively.

- 108. (Previously Presented) The computer program product of claim 107, wherein said removing nonlinearity is carried out by a method comprising
- (a1) calculating an average transformed profile of transformed experiment profiles and transformed reference profiles, wherein each of said transformed

Art Unit: 1631

experiment profiles contains a corresponding said transformed data set  $\{TA_m(k)\}$ , and each of said transformed reference profiles contains a corresponding said transformed data set  $\{TC_m(k)\}$ ; and

(a2) calculating first differences between each of said transformed experiment profiles and said average transformed profile; calculating second differences between each of said transformed reference profiles and said average transformed profile; adjusting, wherein the adjusting comprises correcting nonlinearity each of said transformed experiment profiles based on said first differences between each of said transformed experiment profiles and said average transformed profile, and adjusting, wherein the adjusting comprises correcting nonlinearity each of said transformed reference profiles based on said second differences between each of said transformed reference profiles and said average transformed profile.

109. (Currently Amended) The computer program product of claim 108, wherein the method further comprises calculating said first differences based on the differences in a first subset of error model based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents between each of said transformed experiment profiles and said average transformed profile, and calculating said second differences based on the differences in a second subset of error model based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents

Art Unit: 1631

between each of said transformed reference profiles and said average transformed profile.

wherein each said first subset consists of error-model-based transformed

measurements or logarithm-based transformed measurements that are ranked
similarly between each of said transformed experiment profiles and said average
transformed profile, and each said second subset consists of error-model-based

transformed measurements or logarithm based transformed measurements that are
ranked similarly between each of said transformed reference profiles and said average
transformed profile.

111. (Currently Amended) The computer program product of claim 110, wherein said adjusting step (a2) is carried out by a method comprising:

(a2i) binning said first subset into a plurality of bins, each said bin consisting of error model-based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents in one of said transformed experiment profiles and said average transformed profile having a value in a given range; and binning said second subset into a plurality of bins, each said bin consisting of error-model-based-transformed measurements or logarithm based transformed measurements of said plurality of different cellular constituents in one of said transformed reference profiles and said average transformed profile having a value in a given range;

Application/Control Number: 10/800,340

Art Unit: 1631

and computing corrected error-model-based-transformed measurements of said plurality of different cellular constituents in each said transformed data set  $\{TC_m(k)\}$ , according to the equation:

Page 60

$$TC_{m}^{CQTT}(k) = TC_{m}(k)$$
 -  $nonlinear \_TC_{m}(k)$ ,

where k = 1, ..., N; and where  $\{TA \frac{corr}{m}(k)\}$  is said first processed data set of said processed experiment profile  $PA_m$ , and  $\{TC \frac{corr}{m}(k)\}$  is said second processed data set of said processed reference profile  $PC_m$ .

- 112. (Currently Amended) The computer program product of claim 111, wherein said processed experiment profile PA<sub>m</sub> and said processed reference profile PC<sub>m</sub> comprise error model based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents from the same experimental reaction.
- 113. (Currently Amended) The computer program product of claim 112, wherein the method further comprises calculating  $\widetilde{FG}(k)$  according to the equation

$$PC(k) = \frac{1}{N} \sum_{m=1}^{M} PC_{m}(k),$$

wherein  $(PC_m(k))$  comprises error-model-based transformed measurements or logarithm-based transformed measurements from said second processed data set  $\{TC \frac{corr}{m}(k)\}$  and calculating said differential reference profile according to the

Art Unit: 1631

equation

$$PC_{aux}(m,k) = PC_{m}(k) - \overline{PC}(k)$$

and wherein said first error-corrected profile is calculated according to the equation

$$PA'_{m}(k) = PA_{m}(k) - PC_{eff}(m, k),$$

wherein  $\{PA_m(k)\}$  comprises error-model-based-transformed-measurements or logarithm-based transformed measurements from said first data set  $\{TA\frac{corr}{m}(k)\}$ .

- 114. (Previously Presented) The computer program product of claim 113, wherein the method further comprises
- (d) calculating for each processed profile pair  $\{PA_m, PC_m\}$ , where  $m \in \{1, 2, ..., M\}$ , a second error-corrected experiment profile  $PA''_m$  comprising data set  $(PA''_m(k))$  by combining said first error-corrected experiment profile  $PA'_m$  with said processed experiment profile  $PA_m$  using a weighing factor  $\{w(k)\}$ , k = 1, 2, ..., N, wherein w(k) is a weighing factor for the k'th measurement.
- 115. (Previously Presented) The computer program product of claim 114, wherein said second error-corrected experiment profile  $PA''_m$  is calculated according to the equation

$$PA''_{m}(k) = (1-w(k)) \cdot PA_{m}(k) + w(k)PA'_{m}(k).$$

116. (Previously Presented) The computer program product of claim 115, wherein the method further comprises determining said weighing factor according to

Page 62

the equation

$$w(k) = 1 - e^{-0.5 \left[\frac{N^2(k)}{20000000}\right]^2}$$

where avg\_bkgstd is an average background standard error.

117. (Previously Presented) The computer program product of claim 116, wherein the method further comprises determining said avg\_bkgstd according to the equation

$$avg\_bkgstd = \frac{1}{n} \sum_{k=1}^{N} \left[ \frac{1}{n} \sum_{m=1}^{M} bkgstd(m,k) \right]$$

where bkgstd (m, k) is background standard error of  $PC_m(k)$ .

- 118. (Previously Presented) The computer program product of claim 113, wherein the method further comprises determining errors  $\{P\sigma'_m\}$  of said first error-corrected experiment profile  $\{PA'_m\}$ , wherein said  $\{P\sigma'_m\}$  comprises error data set  $\{P\sigma'_m(k)\}$ .
- 119. (Previously Presented) The computer program product of claim 118, wherein the method further comprises determining said error data set  $\{P\sigma'_m(k)\}$  according to the equation

$$\sigma'_{m}(k) = \sqrt{P\sigma_{m}^{2}(k)} = mixed\_P\sigma_{m}^{2}(k) - 2Cor(k) \cdot P\sigma_{m}(k) \cdot mixed\_P\sigma_{m}(k)$$

where  $P\sigma_{m}(k)$  is the standard error of  $A_{m}(k)$ , and determining  $mixed P\sigma_{m}(k)$ 

Application/Control Number: 10/800,340

Art Unit: 1631

according to the equation

$$mixad_P\sigma_m(k) = \frac{v\sigma_m(k) + (N-1)P\sigma_{paf}(k)}{N}$$

where

$$p_{\mathcal{O}_{ref}}(k) = \sqrt{\frac{1}{N-1}} \sum_{m}^{M} (PC_{m}(k) - PC(k))^{3}$$

and where Cor(k) is a correlation coefficient between said processed experiment profile  $PA_m$  and said processed reference profile  $PC_m$ 

Page 63

120. (Previously Presented) The computer program product of claim 119, wherein said Cor(k) is determined according to the equation

$$Cor(k) = CorMax - \left[1 - e^{-0.5\left[\frac{RC(k)}{2000,R(k)}\right]^2}\right]$$

where CorMax is a number between 0 and 1.

- 121. (Previously Presented) The computer program product of claim 120, wherein the method further comprises determining errors  $\{P\sigma^*_{m}\}$  of said second error-corrected experiment profile  $\{PA^*_{m}\}$  wherein said  $\{P\sigma^*_{m}\}$  comprises error data set  $\{P\sigma^*_{m}(k)\}$ .
- 122. (Previously Presented) The computer program product of claim 121, wherein the method further comprises determining said error data set  $\{P\sigma^*_{-m}(k)\}$  according to the equation

Application/Control Number: 10/800,340

Art Unit: 1631

$$P\sigma_{m}^{*}(k) = \sqrt{[1-w(k)] \cdot P\sigma_{m}^{2}(k) + w(k)P\sigma_{m}^{2}(k)}$$

where  $P\sigma_m(k)$  is the standard error of  $PA_m(k)$ , and the method further comprises determining  $P\sigma'_m(k)$  according to the equation

$$P\sigma'_{m}(k) = \sqrt{P\sigma_{m}^{2}(k) + mixed_{-}P\sigma_{m}^{2}(k) - 2 \cdot Cor(k) \cdot P\sigma_{m}(k) \cdot mixed_{-}P\sigma_{m}(k)},$$

and

the method further comprises determining mixed  $Pa_{nn}(k)$  according to the equation

$$mixed_{-}P\sigma_{m}(k) = \frac{P\sigma_{m}(k) + (M-1)\tilde{\varphi}\sigma_{rof}(k)}{M}$$

where

$$P\sigma_{rej}(k) = \sqrt{\frac{1}{M-1}\sum_{m}^{M} (PC_m(k) - PC(k))^2}$$

and where Cor(k) is a correlation coefficient between said processed experiment profile  $PA_m$  and said processed reference profile  $PC_m$ .

123. (Previously Presented) The computer program product of claim 122, wherein the method further comprises determining said Cor(k) according to the equation

$$Cor(k) = CorMax \cdot \left[1 - s^{-0.5 \left[\frac{76(k)}{479.85988d}\right]^2}\right]$$

where CorMax is a number between 0 and 1.

Art Unit: 1631

124. (Previously Presented) The computer program product of claim 123, wherein each said pair of profiles  $XA_m$  and  $XC_m$  comprise measurements of said plurality of different cellular constituents from a two-channel microarray experiment.

- 125. (Previously Presented) The computer program product of claim 124, wherein said reference profiles  $\{XC_m\}$ , m = 1, 2, ..., M, are measured with samples labeled with a same label.
- 126. (Previously Presented) The computer program product of claim 125, wherein at least one of said pairs of profiles {XA<sub>m</sub>, XC<sub>m</sub>} is a virtual profile.
- 127. (Currently Amended) A computer program product for use in conjunction with a computer having a processor and a memory connected to the processor, said computer program product comprising a computer readable storage medium having a computer program mechanism encoded thereon, wherein said computer program mechanism may be loaded into the memory of said computer and cause said computer to carry out a method for generating at least one error-corrected experiment profile of at least one experiment profile  $A_m$ , where  $m \in \{1, 2, ..., M\}$  in at least one of a plurality of pairs of profiles  $\{A_m, C_m\}$ ,  $A_m$  being an experiment profile,  $C_m$  being a reference profile, where m = 1, 2, ..., M, M is the number of pairs of profiles, said method comprising:

Art Unit: 1631

via said a differential reference profile  $C_{diff}(m,k)$  calculated between  $C_m$  and an average reference profile C determined for profile pair  $\{\Lambda_m, C_m\}$  where  $m \in \{1, 2, ...\}$ M, wherein said average reference profile  $\tilde{G}$  comprises data set  $\{\tilde{\mathbf{C}}(k)\}$ . removing, on a computer, systematic cross-experiment error from said experiment profile Am to generate a first error-corrected experiment profile A'm; wherein said average reference profile  $\mathcal{E}$  is an average of reference profiles  $\{C_m\}$ , m=1,2,..., M; wherein for each  $m \in \{1, 2, ..., M\}$ , said first error-corrected experiment profile  $A'_m$  comprises data set  $\{A'_m(k)\}$ , said experiment profile  $A_m$  comprises data set  $\{A_m(k)\}$ , and said reference profile  $C_m$  comprises data set  $\{C_m(k)\}$ , and said average reference profile  $\mathcal{E}$  comprises duta set  $\{\mathcal{E}_{-}(k)\}_{\tau}$  wherein said data set  $\{A_{m}(k)\}$ comprises measurements, error-model-based transformed measurements, or logarithm-based-transformed-measurements of a plurality of different cellular constituents measured in a sample having been subject to a first condition, said data set  $\{C_m(k)\}$  comprises measurements, error model-based transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents measured in a sample having been subject to a second condition, wherein k = 1, 2, ..., N; k is an index of measurements, error modelbased transformed measurements, or logarithm based transformed measurements of cellular constituents, N being the total number of measurements, wherein generating respective A'm (k) of said first error-corrected experiment profile A'm comprises subtracting  $C_{6666}(m,k)$  from  $A_{m}(k)$ ;

Art Unit: 1631

obtaining a data set  $\{A''_{m}(k)\}$ , wherein obtaining said data set  $\{A''_{m}(k)\}$  comprises combining said first error corrected experiment profile  $A'_{m}$  with said experiment profile  $A_{m}$  using a weighing factor  $\{n(k)\}$ , k = 1, 2, ..., N, wherein m(k) is a weighing factor for a kth measurement; and

outputting to a user, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying: said first error-corrected experiment profile  $\Lambda'_{m}[[.]]$  or said data set  $\{\Lambda'_{m}(k)\}$ , wherein said second error-corrected experiment profile  $\Lambda''_{m}$  or said data set  $\{\Lambda''_{m}(k)\}$ , wherein said second error-corrected experiment profile  $\Lambda''_{m}$  comprises said data-set  $\{\Lambda''_{m}(k)\}$ .

128. (Previously Presented) The computer program product of claim 88, wherein the method further comprises obtaining said transformed measurements of said data set  $\{A_m(k)\}$  and said data set  $\{C_m(k)\}$  for an experiment according to the equations:

$$A_{\mathfrak{m}}(k) = f(x) = \frac{2\pi \left[\frac{8^{2} + 2 \cdot \mathbf{g}^{2} \cdot X \mathbf{a}_{\mathfrak{m}}(k)}{6} + 2\sqrt{c^{2} + b^{2} \cdot X \mathbf{a}_{\mathfrak{m}}(k) + c^{2} \cdot [X \mathbf{a}_{\mathfrak{m}}(k)]^{2}}\right]}{a} + d,$$
for  $XA_{\mathfrak{m}}(k) \geq 0$ 

and

$$C_m(k) = f(x) = \frac{\ln \left[\frac{b^2 \times x \cdot a^2 \cdot XC_m(k)}{x} + 2\sqrt{c^2 + b^2 \cdot XC_m(k) + a^2 \cdot [XC_m(k)]^2}\right]}{a} + d,$$
 for  $XC_m(k) > 0$ 

Art Unit: 1631

where  $\{XA_m(k)\}$  and  $\{XC_m(k)\}$  are data sets comprising measurements of said piurality of different cellular constituents that when transformed produce said transformed measurements of said plurality of different cellular constituents of said data set  $A_m(k)$  and said data set  $C_m(k)$ , respectively, where d is described by the equation:

$$d = \frac{\ln \left[\frac{k^2}{a} + 2 \cdot a\right]}{a}$$

and where a is the fractional error coefficient of said experiment, b is the Poisson error coefficient of said experiment, and c is the standard deviation of background noise of said experiment.

129. (Previously Presented) The computer program product of claim 99, wherein said processing comprises:

normalizing, transforming, and/or removing nonlinearity from measurements of said plurality of cellular constituents of said data set  $\{XA_m(k)\}$  of said experiment profile  $XA_m$ , and from measurements of said plurality of cellular constituents of said data set  $\{XC_m(k)\}$  of said reference profile  $XC_m$ .

130. (Currently Amended) A computer system comprising:

a processor; and

a memory coupled to said processor and encoding one or more programs;

Art Unit: 1631

wherein said one or more programs cause the processor to carry out a method for generating at least one error-corrected experiment profile of at least one experiment profile in a plurality of pairs of profiles  $\{A_m, C_m\}$ , where m = 1, 2, ..., M, and M is the number of the pairs of profiles; and wherein, for each  $m \in \{1, 2, ..., M\}$ ,  $A_m$  is an experiment profile, and  $C_m$  is a reference profile; and wherein  $\{A_m\}$  represents experiment profiles in said plurality of pairs of profiles  $\{A_m, C_m\}$  and  $\{C_m\}$  represents reference profiles in said plurality of pairs of profiles  $\{A_m, C_m\}$ , said method comprising:

- (a) calculating, on a computer, an average reference profile  $\mathcal{C}$  of said phrality of reference profiles  $\{C_m\}$  where m=1,2,...,M;
- (b) determining, on a computer, for at least one profile pair  $\{A_m, C_m\}$  where  $m \in \{1, 2, ..., M\}$  of said plurality of pairs of profiles  $\{A_m, C_m\}$  a differential reference profile  $G_{diff}(m,k)$  computed between  $C_m$  and  $G_n$  wherein said average reference profile  $\overline{G}$  comprises data set  $\{\overline{G}(k)\}$ :
- (c) via said differential reference profile determined for said profile pair, removing, on a computer, systematic cross-experiment error from an experiment profile A<sub>m</sub> of said at least one profile pair {A<sub>m</sub>, C<sub>m</sub>} where m ∈ {1, 2, ..., M} to generate a first error-corrected experiment profile A'<sub>m</sub> for each m ∈ {1, 2, ..., M}, wherein said experiment profile A<sub>m</sub> comprises a first data set(Δ<sub>m</sub>(k)), said reference profile C<sub>m</sub> comprises a second data set, said average reference profile C comprises data set {C (li)}, and said first error-corrected experiment profile A'<sub>m</sub> comprises data set {A'<sub>m</sub>(k)};

Art Unit: 1631

wherein said first data set comprises measurements, or ror-model-based transformed measurements, or logarithm-based transformed in a sample having been subject to a first condition, said second data set comprises measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents measured in a sample having been subject to a second condition; and wherein k = 1, 2, ..., N; k is an index of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements, or logarithm-based transformed measurements, or logarithm-based transformed measurements, wherein said first error-corrected experiment profile  $A'_m$  is generated according to the equation  $A'_m(k) = A_m(k) - C_{dist}(m,k)$ ; and

- (d) obtaining a data set  $\{A''_m(k)\}$ , wherein obtaining said data set  $\{A''_m(k)\}$  comprises combining said first error-corrected experiment profile  $A'_m$  with said experiment profile  $A_m$ -using a weighing factor  $\{w(k)\}$ ,  $k=-1,2,\ldots,N$ , wherein w(k) is a weighing factor for a k'th measurement; and
- (e) (d) outputting to a user, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying; said first error-corrected experiment profile A'<sub>m</sub>[[,]] or said data set {A'<sub>m</sub>(k)}, a second error-corrected experiment profile A''<sub>m</sub> or said data set {A''<sub>m</sub>(k)}, wherein said second error-

Art Unit: 1631

corrected experiment profile  $A^{**}_{m}$ -comprises said data-set  $\{A^{n}_{m}(k)\}$ .

131. (Previously Presented) The computer system of claim 130, wherein said steps (b) and (c) are performed for each profile pair  $\{A_m, C_m\}$  where  $m \in \{1, 2, ..., M\}$ .

- 132. (Currently Amended) The computer system of claim 131, wherein each of said experiment profile A<sub>m</sub> and said reference profile C<sub>m</sub> comprises measurements; error model based transformed measurements; or logarithm based transformed measurements of said plurality of different cellular constituents from the same experimental reaction.
- 133. (Previously Presented) The computer system of claim 132, wherein said  $\tilde{C}(k)$  is calculated according to the equation

$$\mathcal{C}(k) = \frac{1}{M} \sum_{m=1}^{M} C_m(k)$$

Wherein said differential reference profile is determined according to the equation

$$C_{aijj}(m,k) = C_m(k) - \tilde{C}(k)$$

and wherein said first error-corrected experiment profile  $A^{\prime}_m$  is generated according to the equation

Art Unit: 1631

$$A'_{m}(k) - A_{m}(k) - C_{mff}(m,k)$$

wherein  $\{A_m(k)\}$  is said first data set of experiment profile  $A_m$ .

134. (Currently Amended) The computer system of claim 133, wherein the method further comprises:

- (d) (e) calculating, for one or more remaining profile pairs out of said profile pairs  $\{A_m, C_m\}$ , a respective second error-corrected experiment profile  $A''_m$ ; and
- (e)  $(\underline{\Omega})$  outputting to, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying; said respective second error-corrected experiment profile  $A''_m$  or said  $\underline{a}$  data set  $\{A''_m(k)\}$ .
- 135. (Previously Presented) The computer system of claim 134, wherein said second error-corrected experiment profile A" is calculated according to the equation

$$A''_{ma}(k) = (1-w(k)) \cdot A_m(k) + w(k) \cdot A'_{ma}(k).$$

136. (Currently Amended) The computer system of claim 135, wherein the method further comprises determining said a weighing factor w(k) according to the equation

Art Unit: 1631

where avg hkgstd is an average background standard error.

137. (Previously Presented) The computer system of claim 136, wherein the method further comprises determining said ava blastd according to the equation

$$avg\_bkystd = \frac{1}{N} \sum_{k=1}^{N} \left[ \frac{1}{N} \sum_{m=1}^{M} bkgstd(m,k) \right]$$

where bkgstd (m, k) is background standard error of  $C_m(k)$ .

- 138. (Previously Presented) The computer system of claim 133, wherein the method further comprises determining errors  $\{\sigma'_m(k)\}$  of said data set  $\{A'_m(k)\}$  in said first error-corrected experiment profile  $A'_m$ .
- 139. (Previously Presented) The computer system of claim 138, wherein the method further comprises determining said errors  $\{\sigma'_{sr}(k)\}$  according to the equation

$$\sigma'_{m}(k) = \sqrt{\sigma_{m}^{2}(k) + mixed_{m}\sigma_{m}^{2}(k) - 2 \cdot Cor(k) \cdot \sigma_{m}(k) \cdot mixed_{m}\sigma_{m}(k)}$$

where  $\sigma_m$  (k) is the standard error of  $A_m(k)$ , the method further comprising determining  $mixed \ \sigma_m$  (k) according to the equation

$$mixed_\sigma_m(k) = \frac{\sigma_m(k) + (k-1)\sigma_{ref}(k)}{M}$$

where 
$$\sigma_{ref}(k) = \sqrt{\frac{1}{N-1}} \sum_{m}^{N} (C_m(k) - C(k))^2$$

Art Unit: 1631

and where Cor(k) is a correlation coefficient between said experiment profile  $A_m$  and said reference profile  $C_m$ .

140. (Previously Presented) The computer system of claim 139, wherein the method further comprises determining said Cor(k) according to the equation

$$Cor(k) = CorMax \cdot \left[1 - e^{-0.5 \cdot \left[\frac{\tilde{c}(k)}{arg, \tilde{c}(k)}\right]^2}\right]$$

where CorMax is a number between 0 and 1.

- 141. (Previously Presented) The computer system of claim 136, wherein the method further comprises determining errors  $\{\sigma^*_{m}(k)\}$  of said data set  $\{A''_{m}(k)\}$  in said second error-corrected experiment profile  $A''_{m}$ .
- 142. (Previously Presented) The computer system of claim 141, wherein said errors  $\{\sigma^*_{-\infty}(k)\}$  are determined according to the equation

$$\sigma''_{m}(k) = \sqrt{[1 - w(k)] \cdot \sigma_{m}^{2}(k) + w(k) {\sigma'_{m}}^{2}(k)}$$

where  $\sigma_m(k)$  is the standard error of  $A_m(k)$ , the method further comprising (i) determining  $\sigma'_m(k)$  according to the equation

$$\sigma'_{m}(k) = \sqrt{\sigma_{m}^{2}(k) + mixed \sigma_{m}^{2}(k) - 2 \cdot Cor(k) \cdot \sigma_{m}(k) \cdot mixed \sigma_{m}(k)}, \text{ and}$$

(ii) determining  $mixed \ \sigma_m(k)$  according to the equation

Art Unit: 1631

$$mixnd\_\sigma_m(k) = \frac{\sigma_{m}(k) + (M-1) + \sigma_{mef}(k)}{M}$$
 where 
$$\sigma_{mef}(k) = \sqrt{\frac{1}{M-1} \sum_{m} (c_m(k) - C(k))^2}$$

and where Cor(k) is a correlation coefficient between said experiment profile  $A_m$  and said reference profile  $C_m$ .

143. (Previously Presented) The computer system of claim 142, wherein the method further comprises determining said Cor(k) according to the equation

$$Cor(k) = CorMax \cdot \left[1 - e^{-0.5 \left[\frac{\tilde{G}(0)}{4\pi (8.8860004)}\right]^2}\right]$$

where CorMax is a number between 0 and 1.

- 144. (Previously Presented) The computer system of claim 131, wherein said experiment profile  $A_m$  and said reference profile  $C_m$  of each said profile pair  $\{A_m, C_m\}$  are measured in a two-channel microarray experiment.
- 145. (Previously Presented) The computer system of claim 144, wherein said reference profiles  $\{C_m\}$ , where m-1, 2, ..., M, are measured with samples labeled with a same label.

Art Unit: 1631

146. (Previously Presented) The computer system of claim 131, wherein at least one of said plurality of pairs of profiles  $\{A_{sn}, C_m\}$  is a virtual profile.

- 147. (Currently Amended) The computer system of claim 130, wherein said pinrality of pairs of profiles  $\{A_m, C_m\}$  are transformed profiles each comprising error model based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents in data set  $\{A_m(k)\}$  and data set  $\{C_m(k)\}$ , respectively; and wherein said data set  $\{A_m(k)\}$  is said first data set, and said data set  $\{C_m(k)\}$  is said second data set.
- 148. (Currently Amended) The computer system of claim 130, wherein the method further comprises:
- (a0) removing nonlinearity, prior to said calculating step (a), from measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents to generate said plurality of pairs of profiles {A<sub>m</sub>, C<sub>m</sub>} comprising said experiment profile A<sub>m</sub> and reference profile C<sub>m</sub>.
- 149. (Currently Amended) The computer system of claim 148, wherein said removing step (a0) comprises:
- (a0i) calculating an average profile of pre-experiment profiles  $(A \frac{pre}{m})$  and pre-reference profiles  $\{C \frac{pre}{m}\}$ ; wherein each of said pre-experiment profiles

Art Unit: 1631

logarithm based transformed measurements of said plurality of different cellular constituents measured in said sample having been subject to said first condition, which when nonlinearity is removed therefrom, produces each said experiment profile A<sub>m</sub>; and wherein each of said pre-reference profiles comprises measurements; error model-based transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents measured in said sample having been subject to said second condition, which when nonlinearity is removed therefrom, produces each said reference profile C<sub>m</sub>; and

(a0ii) calculating first differences between each of said pre-experiment profiles  $\{A_m^{pre}\}$  and said average profile; calculating second differences between each of said pre-reference profiles  $\{C_m^{pre}\}$  and said average profile; adjusting, wherein the adjusting comprises correcting nonlinearity, each of said pre-experiment profiles  $\{A_m^{pre}\}$  based on said first differences between each of said pre-experiment profiles  $\{A_m^{pre}\}$  and said average profile, thereby generating each said experiment profile  $A_m$ ; and adjusting, wherein the adjusting comprises correcting nonlinearity, each of pre-reference profiles  $\{C_m^{pre}\}$  based on said second differences between each of said pre-reference profiles  $\{C_m^{pre}\}$  and said average profile, thereby generating each said reference profile  $\{C_m^{pre}\}$  and said average profile, thereby

Art Unit: 1631

150. (Currently Amended) The computer system of claim 149, wherein the method further comprises calculating said first differences based on a first subset of said measurements, error-model-based transformed measurements, or logarithm-based-transformed-measurements of said plurality of different cellular constituents in said pre-experiment profiles  $\langle A|\frac{pre}{m}\rangle$  and said average profile; and calculating said second differences based on a second subset of said measurements, error-model-based-transformed-measurements, or logarithm-based-transformed measurements of said plurality of different cellular constituents in said pre-reference profiles  $\{C|\frac{pre}{m}\}$  and said average profile.

- said first subset consists of measurements, error-model-based transformed measurements, or logarithm-based-transformed measurements of said plurality of different cellular constituents that are ranked similarly between each of said pre-experiment profiles  $\{A_{in}^{pre}\}$  and said average profile, and said second subset consists of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents that are ranked similarly between each of said pre-reference profiles  $\{C_{in}^{pre}\}$  and said average profile.
  - 152. (Currently Amended) The computer system of claim 151, wherein

Art Unit: 1631

said adjusting step (a0ii) is carried out by a method comprising:

(iii) binning said first subset into a first plurality of bins, wherein each of said first plurality of bins consists of measurements, error-model based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in one of said pre-experiment profiles  $\{A_{m}^{pre}\}$  and said average profile having a value in a given range; and binning said second subset into a second plurality of bins, wherein each of said second plurality of bins consists of measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in one of said pre-reference profiles  $\{C_{m}^{pre}\}$  and said average profile having a value in a given range;

- (ii2) calculating, in each bin of said first plurality of bins, a first mean difference between a feature value of measurements, error-model-based transformed measurements, or logarithm based transformed measurements of said one of said pre-experiment profiles  $\{A_{m}^{pre}\}$  and a feature value of said average profile, and calculating a second mean difference between a feature value of measurements, error-model-based transformed measurements, or logarithm based transformed-measurements of said one of said pre-reference profiles  $\{C_{m}^{pre}\}$  and a feature value of said average profile;
- (ii3) determining a first curve of said first mean difference as a first function of values of measurements, error-model-based transformed measurements, or

Art Unit: 1631

logarithm-based transformed-measurements of said phrality of different cellular constituents for said one of said pre-experiment profiles  $\{A_m^{pre}\}$ , wherein said first function is represented by, nonlinear  $A_m^{pre}$ ; and determining a second curve of said second mean difference as a second function of values of measurements, errormodel based transformed measurements, or logarithm-based-transformed measurements of said plurality of different cellular constituents for said one of said pre-reference profiles  $\{C_m^{pre}\}$ , wherein said second function is represented by nonlinear  $C_m^{pre}$ ; and

(ii4) adjusting each of said pre-experiment profiles  $\{A\frac{pre}{m}\}$  according to the equation:

$$A_m(k) = A \frac{pre}{m}(k) - nonlinear A \frac{pre}{m}(k)$$

and adjusting each of said pre-reference profiles  $\{C^{pre}_{m}\}$  according to the equation:

$$C_m(k) = C \frac{pre}{m}(k) - nonlinear \_C \frac{pre}{m}(k),$$

where  $k=1,\ldots,N$ ; and where  $A\frac{pre}{m}(k)$  and  $C\frac{pre}{m}(k)$  are data sets of each of said pre-experiment profiles  $\{A\frac{pre}{m}\}$  and each of said pre-reference profiles  $\{C\frac{pre}{m}\}$ , respectively; and where  $A_m(k)$  and  $C_m(k)$  are said first data set and said second data set, respectively.

153. (Currently Amended) The computer system of claim 130, wherein

Art Unit: 1631

the method further comprises:

(a0) normalizing, prior to said calculating step (a), measurements, errormodel-based transformed measurements, or logarithm based transformed measurements of said plurality of different cellular constituents in a pre-experiment profile  $A_m^{pre}$  and a pre-reference profile  $C_m^{pre}$  to generate said experiment profile  $A_m$  and said reference profile  $C_m$  respectively.

154. (Currently Amended) The computer system of claim 153, wherein said normalizing step (a0) comprises normalizing a data set  $A_{m}^{pre}(k)$  and a data set  $C_{m}^{pre}(k)$ , according to the equations:

$$A_{m}(k) = \frac{k^{pro}(k) \cdot k^{pro} \cdot c^{pro}}{4^{pro}}$$

and

$$C_m(k) = \frac{c^{pre}(x) \cdot x^{pre} \cdot \overline{c^{pre}}}{2m},$$

wherein said data sets  $A_{m}^{pre}(k)$  and  $C_{m}^{pre}(k)$  each comprises measurements, errormodel-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents, where  $A_{m}^{pre}$  is an average of measurements, error-model-based-transformed-measurements, or logarithm-based\_transformed-measurements of said plurality of different cellular constituents in said  $A_{m}^{pre}(k)$ , and  $\overline{C_{m}^{pre}}$  is an average of measurements, error-model-

Art Unit: 1631

$$\overline{A_{m}^{pro}C_{m}^{pro}} = \frac{1}{2K} \sum_{m=1}^{M} \overline{(A_{m}^{pro} + \overline{C_{m}^{pro}})}.$$

155. (Previously Presented) The computer system of claim 154, wherein the method further comprises normalizing errors of said data sets  $\{A_m^{pre}(k)\}$  and  $\{C_m^{pre}(k)\}$ , respectively, according to the equations:

$$\sigma \frac{NA}{m}(k) = \frac{\sigma^{\text{pred}}(k) \cdot \lambda^{\text{pre}} c^{\text{pre}}}{\frac{\lambda^{\text{pre}}}{m}}$$

and

$$\sigma \frac{NC}{m}(k) = \frac{\sigma^{pred}(k) \tilde{A}^{pre} \frac{\partial}{\partial r^{pre}}}{\sigma^{pre}},$$

Art Unit: 1631

where  $\sigma \frac{preA}{m}(k)$  and  $\sigma \frac{preC}{m}(k)$  are the standard errors of  $A \frac{pre}{m}(k)$  and  $C \frac{pre}{m}(k)$ , respectively, and  $\sigma \frac{NA}{m}(k)$  and  $\sigma \frac{NC}{m}(k)$  are normalized standard errors of  $A_m(k)$  and  $C_m(k)$ , respectively.

156. (Previously Presented) The computer system of claim 155, wherein the method further comprises normalizing background errors of said data sets  $\{A_{m}^{pre}(k)\}$  and  $\{C_{m}^{pre}(k)\}$ , respectively, according to the equations:

$$bkgstd \stackrel{NA}{=}(k) = \frac{bkgstd}{m} \frac{greA_{(k),A}pre}{m} \frac{pre}{m} \frac{greA_{(k),A}pre}{m}$$

and

$$bkgstd \stackrel{\mu_{\mathcal{C}}}{=}(k) = \frac{bkgstd \frac{\mu_{\mathcal{C}}(k)}{R} \frac{\lambda^{\mu_{\mathcal{C}}(k)}}{R} \frac{\mu_{\mathcal{C}}(k)}{R}}{C^{\mu_{\mathcal{C}}(k)}}$$

where  $bkgstd \frac{preA}{m}(k)$  and  $bkgstd \frac{preC}{m}(k)$  are the standard background errors of  $A^{pre}_{m}(k)$  and  $C^{pre}_{m}(k)$ , respectively, and  $bkgstd \frac{NA}{m}(k)$  and  $bkgstd \frac{NC}{m}(k)$  are normalized standard background errors of  $A_{m}(k)$  and  $C_{m}(k)$ , respectively.

157. (Currently Amended) The computer system of claim 156, wherein the method further comprises calculating said averages  $\overline{A}_{m}^{\overline{pre}}$  and  $\overline{C}_{m}^{\overline{pre}}$  by excluding measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents having

Art Unit: 1631

a value among the highest 10% of said measurements, error-model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents in said data sets  $(A_{m}^{pre}(k))$  and  $\{C_{m}^{pre}(k)\}$ , respectively.

158. (Currently Amended) A computer system comprising:

a processor; and

a memory coupled to said processor and encoding one or more programs; wherein said one or more programs cause the processor to carry out a method for generating at least one error-corrected experiment profile of at least one experiment profile in a plurality of pairs of profiles  $\{XA_{m}, XC_{m}\}$ ,  $XA_{m}$  being an experiment profile,  $XC_{m}$  being a reference profile, where m = 1, 2, ..., M, M is the number of pairs of profiles, said method comprising:

- (a) processing, on a computer, said plurality of pairs of profiles {XA<sub>m</sub>, XC<sub>m</sub>} to obtain a plurality of pairs of processed profiles {PA<sub>m</sub>, PC<sub>m</sub>}, PA<sub>m</sub> being a processed experiment profile, PC<sub>m</sub> being a processed reference profile, wherein said processing comprises normalizing at least one said experiment profile XA<sub>m</sub> and reference profile XC<sub>m</sub>:
- (b) calculating, on a computer, an average processed reference profile PC of processed reference profiles  $\{PC_m\}$ , where m = 1, 2, ..., M;
  - (c) determining, on a computer, for at least one processed profile pair  $\{PA_{\pi s}\}$

Art Unit: 1631

 $PC_m$ } where  $m \in \{1, 2, ..., M\}$  of said plurality of pairs of processed profiles  $\{PA_m, PC_m\}$ , where m = 1, 2, ..., M, a differential reference profile  $\underline{PC_{diff}(m,k)}$  computed between  $PC_m$  and  $\underline{PC_m}$  wherein said average processed reference profile  $\underline{PC_m}$  comprises data set  $\{\underline{PC_m}(k)\}$ ;

(d) via said differential reference profile determined for said at least one processed profile pair, removing, on a computer, systematic cross-experiment error from a processed experiment profile PA<sub>m</sub> of said at least one processed profile pair {PA<sub>m</sub>,  $PC_m$  where  $m \in \{1, 2, ..., M\}$  to generate a first error-corrected processed experiment profile PA'<sub>m</sub>; wherein for each m € {1, 2, ..., M}, said processed experiment profile  $PA_m$  comprises a first processed data set  $\{PA_m(k)\}$ , said processed reference profile PC<sub>m</sub> comprises a second processed data set, said average-processed-reference-profile FC comprises data set (FC(k)), said first error-corrected processed experiment profile PA'm comprises dataset {PA'm (k)}, said experiment profile XA, comprises data set {XA, (k)}, said reference profile XC, comprises data set  $\{XC_m(k)\}$ , wherein said data set  $\{XA_m(k)\}$  comprises measurements of a plurality of different cellular constituents measured in a sample having been subject to a first condition, said data set  $\{XC_m(k)\}$  comprises measurements of said plurality of different cellular constituents measured in a sample having been subject to a second condition, and where k = 1, 2, ..., N; k is an index of measurements of cellular constituents. N being the total number of measurements, wherein said first error-corrected processed experiment profile

Art Unit: 1631

телентение<del>л\</del>телен

(f) (e) outputting to a user, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying: said first error-corrected processed experiment profile PA'<sub>m</sub> [[.]] or said data set {PA'<sub>m</sub> (k)} -w second error-corrected processed experiment profile PA''<sub>m</sub> or said data set {PA''<sub>m</sub> (k)}, wherein said second error-corrected processed experiment profile PA''<sub>m</sub> comprises said data set {PA''<sub>m</sub> (k)}.

- 159. (Previously Presented) The computer system of claim 158, wherein said processing step (a) comprises normalizing each said experiment profile  $XA_m$  and reference profile  $XC_m$ .
- 160. (Currently Amended) The computer system of claim 159, wherein said normalizing is carried out according to the equations:

$$NA_{m}(k) = \frac{XA_{m}(k) \cdot XAC}{XX_{m}}$$

and

$$NC_m(k) = \frac{\pi c_m(k) \cdot \pi k \overline{k}}{\Re \Sigma_m}$$

where  $\{NA_m(k)\}$  is said first data set of said processed experiment profile  $PA_m$ , and  $\{NC_m(k)\}$  is said second data set of said processed reference profile  $PC_m$ ; where  $XA_m$  is an average of measurements, error model-based transformed measurements, or logarithm-based transformed measurements of said pharality of different cellular constituents of said data set  $\{XA_m(k)\}$ , and  $\overline{XC_m}$  is an average of measurements, error model-based transformed measurements, or logarithm-based transformed measurements of said pharality of different cellular constituents of data set  $\{XC_m(k)\}$ ; and wherein XXC is an average calculated according to the equation

$$XXC = \frac{1}{2M} \sum_{m=1}^{M} (XA_m + XC_m).$$

161. (Previously Presented) The computer system of claim 160, wherein the method further comprises normalizing errors of said experiment profile  $XA_m$  and reference profile  $XC_m$  according to the equations:

$$\sigma_{m}^{A}(k) = \frac{\sigma^{XA}(k) \cdot XK}{XA_{m}}$$

and

$$\sigma_{m}^{C}(k) = \frac{\pi C_{m}}{2}$$

where  $\sigma_{m}^{XA}(k)$  and  $\sigma_{m}^{XC}(k)$  are the standard errors of  $XA_{m}(k)$  and  $XC_{m}(k)$ ,

Application/Control Number: 10/800,340

Art Unit: 1631

respectively, and  $\sigma_m^A(k)$  and  $\sigma_m^C(k)$  are normalized standard errors of  $NA_m(k)$  and  $NC_m(k)$ , respectively.

162. (Previously Presented) The computer system of claim 161, wherein the method further comprises normalizing background errors of said experiment profile XA<sub>m</sub> and reference profile XC<sub>m</sub> according to the equations:

$$bkgstd\frac{A}{m}(k) = \frac{bkgmn}{m} \frac{XA_{(k)}\overline{XSC}}{XA_{m}}$$

and

$$bkgstd_{\overline{M}}^{C}(k) = \frac{akgstd_{\overline{M}}^{XC}(k)\overline{AC}}{\overline{XC_{max}}}$$

where  $bkgstd\frac{XA}{m}$  (k) and  $bkgstd\frac{XC}{m}$ (k) are the standard background errors of  $XA_m(k)$  and  $XC_m(k)$ , respectively, and  $bkgstd\frac{A}{m}$ (k) and  $bkgstd\frac{C}{m}$ (k) are normalized standard background errors of said  $NA_m(k)$  and said  $NC_m(k)$ , respectively.

163. (Currently Amended) The computer system of claim 161, wherein the method further comprises determining said averages  $\overline{XA_m}$  and  $\overline{XC_m}$  excluding measurements of said plurality of different cellular constituents having a value among the highest 10% of said measurements, experimed based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular

Art Unit: 1631

constituents in said data sets  $(XA_m(k))$  and  $(XC_m(k))$ , respectively.

164. (Previously Presented) The computer system of claim 158, wherein said processing step (a) comprises:

normalizing each said experiment profile  $XA_m$  and reference profile  $XC_m$  to generate normalized data set  $\{NA_m(k)\}$  and normalized data set  $\{NC_m(k)\}$ , respectively;

transforming said normalized data set  $\{NA_m(k)\}$  to obtain a transformed data set  $\{TA_m(k)\}$ , where said transformed data set  $\{TA_m(k)\}$  is said first data set of said processed experiment profile  $PA_m$ ; and

transforming said normalized data set  $\{NC_m(k)\}$  to obtain a transformed data set  $\{TC_m(k)\}$ , where said transformed data set  $\{TC_m(k)\}$  is said second data set of said processed reference profile  $PC_m$ ;

wherein said transforming is carried out for an experiment according to equations

$$TA_{m}(k) = f(x) = \frac{\ln\left[\frac{b^{2} + 2 - w^{2} - 3 A_{m}(k)}{a} + 2 \cdot \sqrt{c^{2} + b^{2} \cdot N A_{m}(k) + a^{2} \cdot (N A_{m}(k))^{2}}\right]}{a} + d,$$
 for  $NA_{m}(k) \ge 0$ 

and

$$TC_{m}(k) = f(x) = \frac{2n \left[\frac{8^{2} + 2 \cdot 6^{2} \cdot NC_{m}(k)}{2} + 2\sqrt{6^{2} + b^{2} \cdot NC_{m}(k)} + a^{2} \cdot NC_{m}(k)\right]^{2}}{n} + d,$$
 for  $NC_{m}(k) > 0$ 

where d is described by equation

Art Unit: 1631

and where a is the fractional error coefficient of said experiment, b is the Poisson error coefficient of said experiment, and a is the standard deviation of background noise of said experiment.

## 165. (Canceled)

166. (Previously Presented) The computer system of claim 158, wherein said processing step (a) comprises:

normalizing each said experiment profile  $XA_m$  and reference profile  $XC_m$  to generate normalized data set  $\{NA_m(k)\}$  and normalized data set  $\{NC_m(k)\}$ , respectively;

transforming said normalized data set  $\{NA_m(k)\}$  to obtain a transformed data set  $\{TA_m(k)\}$ ;

transforming said normalized data set  $\{NC_m(k)\}$  to obtain a transformed data set  $\{TC_m(k)\}$ ; and

removing nonlinearity from each said transformed data sets  $\{TA_m(k)\}$  and  $\{TC_m(k)\}$ , respectively;

wherein said transforming is carried out for an experiment according to equations

$$TA_{m}(k) = f(x) = \frac{\ln \left[ \frac{h^{2} + 2 \cdot e^{2} \cdot NAm(k)}{a} + 2 \cdot \sqrt{e^{2} \cdot h^{2} \cdot NA_{m}(k) + a^{2} \cdot (nA_{m}(k))^{2}} \right]}{a} + d,$$
 for  $NA_{m}(k) > 0$ 

and

Application/Control Number: 10/800,340

Art Unit: 1631

$$TC_{m}(k) - f(x) = \frac{\ln\left[\frac{k^{2} + 2 - x^{2} NC_{m}(k)}{\delta} + 2 \sqrt{e^{2} + b^{2} NC_{m}(k) + a^{2} \sqrt{k^{2} + b^{2}} NC_{m}(k)}\right]}{a} + d,$$
for  $NC_{m}(k) > 0$ 

Page 91

where d is described by equation

and where a is the fractional error coefficient of said experiment, b is the Poisson error coefficient of said experiment, and c is the standard deviation of background noise of said experiment.

- 167. (Currently Amended) The computer system of claim 166, wherein said removing nonlinearity is carried out by a method comprising
- (al) calculating an average transformed profile of transformed experiment profiles and transformed reference profiles, wherein each of said transformed experiment profiles contains a corresponding error model-based transformed or logarithm based transformed data set {TA<sub>m</sub>(k)}, and each of said transformed reference profiles contains a corresponding error model-based transformed measurements or logarithm-based transformed data set {TC<sub>m</sub>(k)}; and
- (a2) calculating first differences between each of said transformed experiment profiles and said average transformed profile; calculating second differences between each of said transformed reference profiles and said average transformed profile; adjusting, wherein the adjusting comprises correcting nonlinearity each of said transformed experiment profiles based on said first

Art Unit: 1631

differences between each of said transformed experiment profiles and said average transformed profile, and adjusting, wherein the adjusting comprises correcting nonlinearity each of said transformed reference profiles based on said second differences between each of said transformed reference profiles and said average transformed profile.

- 168. (Previously Presented) The computer system of claim 167, wherein the method further comprises calculating said first differences based on the differences in a first subset of error model-based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents between each of said transformed experiment profiles and said average transformed profile, and calculating said second differences based on the differences in a second subset of error model based transformed measurements, or logarithm-based transformed measurements of said plurality of different cellular constituents between each of said transformed reference profiles and said average transformed profile.
- 169. (Previously Presented) The computer system of claim 168, wherein each said first subset consists of transformed measurements that are ranked similarly between each of said transformed experiment profiles and said average transformed profile, and each said second subset consists of transformed measurements that are ranked similarly between each of said transformed reference profiles and said average transformed profile.

Art Unit: 1631

170. (Currently Amended) The computer system of claim 169, wherein said adjusting step (a2) is carried out by a method comprising:

(a2i) binning said first subset into a planality of bins, each said bin consisting of error-model-based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents in one of said transformed experiment profiles and said average transformed profile having a value in a given range; and binning said second subset into a plurality of bins, each said bin consisting of error-model-based transformed measurements or logarithm based transformed measurements of said plurality of different cellular constituents in one of said transformed reference profiles and said average transformed profile having a value in a given range;

between a feature value of error-model-based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents in said one of said transformed experiment profiles and a feature value of said average transformed profile, and calculating a second mean difference between a feature value of error-model-based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents in said one of said reference profiles and a feature value of the average profile;

(a2iii) determining a first curve of said first mean difference as a first function of values of error-model-based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents for said one

Art Unit: 1631

of said transformed experiment profiles, wherein said first function is represented by, nonlinear\_TA<sub>m</sub> and determining a second curve of said second mean difference as a second function of values of excer-model-based transformed measurements or logarithm-based transformed measurements of said plurality of different cellular constituents for said one of said transformed reference profiles, wherein said second function is represented by nonlinear\_TC<sub>m</sub>; and

(a2iv) computing corrected error model-based transformed measurements of said plurality of different cellular constituents in each said transformed data set (TA<sub>m</sub>(k)), according to the equation:

$$TA_{m}^{COTT}(k) = TA_{m}(k) - nonlinear_{m}TA_{m}(k),$$

and computing corrected error-model-based-transformed-measurements or logarithm-based transformed measurements of said plurality of different cellular constituents in each said transformed data set  $\{TC_m(k)\}$ , according to the equation:

$$TC_{m}^{corr}(k) = TC_{m}(k) - nonlinear \_TC_{m}(k),$$

where k = 1, ..., N; and where  $\{TA \frac{corr}{m}(k)\}$  is said first processed data set of said processed experiment profile  $PA_m$ , and  $\{TC \frac{corr}{m}(k)\}$  is said second processed data set of said processed reference profile  $PC_m$ .

171. (Currently Amended) The computer system of claim 170, wherein said processed experiment profile PA<sub>m</sub> and said processed reference profile PC<sub>m</sub> comprise error-model-based-transformed-measurements or logarithm-based transformed

Application/Control Number: 10/800,340

Page 95

Art Unit: 1631

measurements of said plurality of different cellular constituents from the same experimental reaction.

172. (Currently Amended) The computer system of claim 171, wherein the method further comprises calculating PC(k) according to the equation

$$PC(k) = \frac{1}{N} \sum_{n=1}^{M} PC_{nn}(k),$$

wherein  $\{PC_m(k)\}$  comprises error-model-based transformed-measurements-or logarithm-based transformed measurements from said second processed data set  $\{TC\frac{corr}{m}(k)\}$  and calculating said differential reference profile according to the equation

$$PC_{diff}(m,k) = PC_{m}(k) - PC(k)$$

and wherein said first error-corrected profile is calculated according to the equation

$$PA'_{m}(k) = PA_{m}(k) - PC_{diff}(m, k),$$

wherein  $\{PA_m(k)\}$  comprises error model-based transformed-measurements or togarithm-based transformed measurements from said first data set  $\{TA\frac{corr}{m}(k)\}$ .

- 173. (Previously Presented) The computer system of claim 172, wherein the method further comprises
- (d) calculating for each processed profile pair  $\{PA_m, PC_m\}$ , where  $m \in \{1, 2, ..., M\}$ , a second error-corrected experiment profile  $PA''_m$  comprising data set  $\langle PA''_m(k) \rangle$  by

Application/Control Number: 10/800,340

Page 96

Art Unit: 1631

combining said first error-corrected experiment profile  $PA'_m$  with said processed experiment profile  $PA_m$  using a weighing factor  $\{w(k)\}$ , k = 1, 2, ..., N, wherein w(k) is a weighing factor for the kth measurement.

- 174. (Previously Presented) The computer system of claim 173, wherein said second error-corrected experiment profile  $PA''_m$  is calculated according to the equation  $PA''_m(k) = (1-w(k)) \cdot PA_m(k) + w(k)PA'_m(k).$
- 175. (Previously Presented) The computer system of claim 174, wherein the method further comprises determining said weighing factor according to the equation

$$w(k) = 1 - e^{-0.9 \left( \frac{\sqrt{2500}}{\log \log ma} \right)^3}$$

where avg\_bkgstd is an average background standard error.

176. (Previously Presented) The computer system of claim 175, wherein the method further comprises determining said avg\_bkgstd according to the equation

avg\_bkgstd = 
$$\frac{1}{n} \sum_{k=1}^{N} \left[ \frac{1}{n} \sum_{m=1}^{M} bkgstd(m,k) \right]$$

where bkgstd (m, k) is background standard error of  $PC_m$  (k).

177. (Previously Presented) The computer system of claim 172, wherein the method further comprises determining errors  $\{P\sigma'_{m}\}$  of said first error-corrected experiment profile  $\{PA'_{m}\}$ , wherein said  $\{P\sigma'_{m}\}$  comprises error data set  $\{P\sigma'_{m}(k)\}$ .

Art Unit: 1631

178. (Previously Presented) The computer system of claim 177, wherein the method further comprises determining said error data set  $\{P\sigma'_m(k)\}$  according to the equation

$$\sigma'_{m}(k) = \sqrt{P\sigma_{m}^{2}(k) = mixed_{po_{m}^{2}(k) - 2Cor(k) \cdot P\sigma_{m}(k) \cdot mixed_{po_{m}(k)}}$$

where  $P\sigma_m(k)$  is the standard error of  $A_m(k)$ , and determining  $mixed \ P\sigma_m(k)$  according to the equation

$$mixed_P\sigma_m(k) = \frac{p_{\sigma_m(k)+(M-1)\cdot p_{\sigma_{ref}(k)}}}{M}$$

where

$$P\sigma_{ref}(k) = \sqrt{\frac{1}{N-1}\sum_{m}^{N} (PC_{m}(k) - \overline{PC}(k))^{2}}$$

and where Cor(k) is a correlation coefficient between said processed experiment profile  $PA_m$  and said processed reference profile  $PC_m$ .

179. (Previously Presented) The computer system of claim 178, wherein said Cor(k) is determined according to the equation

$$Cor(k) = CorMax \cdot \left[1 - e^{-0.5 \left[\frac{2C_{12}}{1-0.5}\right]^{2}}\right]$$

where CorMax is a number between 0 and 1.

180. (Previously Presented) The computer system of claim 179, wherein the

method further comprises determining errors  $\{P\sigma^*_m\}$  of said second error-corrected experiment profile  $\{PA^*_m\}$  wherein said  $\{P\sigma^*_m\}$  comprises error data set  $\{P\sigma^*_m(k)\}$ .

181. (Previously Presented) The computer system of claim 180, wherein the method further comprises determining said error data set  $\{P\sigma^*_{m}(k)\}$  according to the equation

$$Po_m^n(k) = \sqrt{[1-w(k)] \cdot Po_m^2(k) + w(k)Po_m^2(k)}$$

where  $P\sigma_m(k)$  is the standard error of  $PA_m(k)$ , and the method further comprises determining  $P\sigma'_m(k)$  according to the equation

$$P\sigma'_{m}(k) = \sqrt{P\sigma_{m}^{2}(k) + mixed_{*}P\sigma_{m}^{2}(k) - 2 \cdot Cor(k) \cdot P\sigma_{m}(k) \cdot mixed_{*}P\sigma_{m}(k)}.$$

and

the method further comprises determining  $mixed\_P\sigma_m(k)$  according to the equation

$$mixed_P\sigma_m(k) = \frac{Pa_m(k) + (N-1)Pa_{rot}(k)}{N}$$

where

$$P\sigma_{ref}(k) = \sqrt{\frac{1}{M-1} \sum_{m}^{M} (PC_m(k) - PC(k))^2}$$

and where Cor(k) is a correlation coefficient between said processed experiment profile  $PA_m$  and said processed reference profile  $PC_m$ .

Application/Control Number: 10/800,340

Art Unit: 1631

Page 99

182. (Previously Presented) The computer system of claim 181, wherein the method further comprises determining said Cur(k) according to the equation

$$Cor(k) = CorMax \cdot \left[1 - e^{-0.5 \left(\frac{F\zeta_0}{arg.skgstd}\right)^2}\right]$$

where CorMax is a number between 0 and 1.



- 183. (Previously Presented) The computer system of claim 182, wherein each said pair of profiles XA<sub>ss</sub> and XC<sub>ss</sub> comprise measurements of said plurality of different cellular constituents from a two-channel microarray experiment.
- 184. (Previously Presented) The computer system of claim 183, wherein said reference profiles  $\{XC_m\}$ , m = 1, 2, ..., M, are measured with samples labeled with a same label.
- 185. (Previously Presented) The computer system of claim 184, wherein at least one of said pairs of profiles  $\{XA_m, XC_m\}$  is a virtual profile.
  - 186. (Currently Amended) A computer system comprising:

a processor; and

a memory coupled to said processor and encoding one or more programs;

wherein said one or more programs cause the processor to carry out a method for generating at least one error-corrected experiment profile of at least one

Art Unit: 1631

experiment profile  $A_m$ , where  $m \in \{1, 2, ..., M\}$  in at least one of a plurality of pairs of profiles  $\{A_m, C_m\}$ ,  $A_m$  being an experiment profile,  $C_m$  being a reference profile, where m = 1, 2, ..., M, M is the number of pairs of profiles, said method comprising:

via said a differential reference profile  $C_{ant}(m,k)$  calculated between  $C_m$  and an average reference profile  $\mathcal{C}$  determined for profile pair  $\{A_m, C_m\}$  where  $m \in \{1,0\}, ...$ M}, wherein said average reference profile  $\overline{b}$  comprises data set  $\{\overline{b}(k)\}$ . removing, on a computer, systematic cross-experiment error from said experiment profile Am to generate a first error-corrected experiment profile A'm; wherein said average reference profile C is an average of reference profiles  $\{C_m\}$ , m=1,2,..., M; wherein for each m  $\in \{1, 2, ..., M\}$ , said first error-corrected experiment profile  $A'_{m}$  comprises data set  $\{A'_{m}(k)\}$ , said experiment profile  $A_{m}$  comprises data set  $\{A_m(k)\}$ , and said reference profile  $C_m$  comprises data set  $\{C_m(k)\}$ , and said average reference profile & comprises data set { (k)}, wherein said data set { Am(k)} comprises measurements, error-model-based transformed measurements, or logarithm-based transformed-measurements of a plurality of different cellular constituents measured in a sample having been subject to a first condition, said data set {C, (k)} comprises measurements, error model-based transformed measurements, or logarithm-based transformed-measurements of said plurality of different cellular constituents measured in a sample having been subject to a second condition, wherein k " 1, 2, ..., N; k is an index of measurements, error-modelbased transformed measurements, or logarithm based-transformed measurements

Art Unit: 1631

of cellular constituents, N being the total number of measurements, wherein said first error-corrected experiment profile  $A'_{m}$  is generated according to the equation  $A'_{m}(k) = A_{m}(k) - C_{diff}(m.k)$ ;

obtaining data-set  $\{A^{\mu}_{m}(k)\}$ , wherein obtaining said-data-set  $\{A^{\mu}_{m}(k)\}$  comprises combining said first error corrected experiment profile  $A^{\mu}_{m}$  with said experiment profile  $A_{m}$  using a weighing factor  $\{w(k)\}$ ,  $k=1,2,\ldots,N$ , wherein w(k) is a weighing factor for a k'th measurement; and

outputting to a user, a user interface device, a computer readable storage medium, or a local or remote computer system; or displaying: said first error-corrected experiment profile A'<sub>m</sub>[[.]] or said data set {A'<sub>m</sub>(k)}, a second error-corrected experiment profile A''<sub>m</sub>, or said data set {A''<sub>m</sub>(k)}, wherein said second error-corrected experiment profile A''<sub>m</sub> comprises said data set {A''<sub>m</sub>(k)}.

187. (Previously Presented) The computer system of claim 147, wherein the method further comprises obtaining said error-model-based transformed measurements of said data set  $\{A_m(k)\}$  and said data set  $\{C_m(k)\}$  for an experiment according to the equations:

$$A_{m}(k) = f(x) = \frac{i\pi^{\left[\frac{x^{2}+2\cdot\alpha^{2}\cdot XA_{m}(k)}{4} + 2\sqrt{c^{2}+b^{2}\cdot XA_{m}(k) + \alpha^{2}\cdot [VA_{m}(k)]^{2}}\right]}{\alpha} + d,$$
 for  $XA_{m}(k) > 0$ 

and

Art Unit: 1631

$$C_{m}(k) = f(x) = \frac{i\pi \left[\frac{k^{2} + 2 \cdot n^{2} \cdot XC_{m}(k)}{n} + 2 \cdot \sqrt{c^{2} + b^{2} \cdot XC_{m}(k) + a^{2} \cdot XC_{m}(k)}\right]}{a} + d,$$
for  $XC_{m}(k) > 0$ 

where  $\{XA_m(k)\}$  and  $\{XC_m(k)\}$  are data sets comprising measurements of said plurality of different cellular constituents that when transformed produce said error-model-based transformed measurements of said plurality of different cellular constituents of said data set  $A_m(k)$  and said data set  $C_m(k)$ , respectively, where d is described by the equation:

$$d = \frac{-2a\left[\frac{b^2}{a} + 3 - c\right]}{a}$$

and where a is the fractional error coefficient of said experiment, b is the Poisson error coefficient of said experiment, and c is the standard deviation of background noise of said experiment.

188. (Previously Presented) The computer system of claim 158, wherein said processing comprises:

normalizing, transforming, and/or removing nonlinearity from measurements of said plurality of cellular constituents of said data set  $\{XA_m(k)\}$  of said experiment profile  $XA_m$ , and from measurements of said plurality of cellular constituents of said data set  $\{XC_m(k)\}$  of said reference profile  $XC_m$ .

Art Unit: 1631

The following is an examiner's statement of reasons for allowance:

No art shows a differential reference profile computed between reference profiles and an average reference profile, and producing an error-corrected experiment profile by subtracting the differential reference profile from experiment.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

## Conclusion

Claims 1-18, 20-30, 32-36, 38-57, 66, 67, 70-105, 107-164 and 166-188 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1631

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LDR/ Larry Riggs Examiner, Art Unit 1631

/Marjorie Moran/ Supervisory Patent Examiner, Art Unit 1631